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STUDIES OF THE SMALL INTESTINE

II. THE EFFECT OF FOODS AND VARIOUS PATHOLOGIC STATES ON THE GASTRIC EMPTYING AND THE SMALL INTESTINAL PATTERN¹

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SOME years ago Halsted made the statement that all that is thought new in medicine may not be new but merely rediscovery and elaboration. The major advances in medical knowledge are rarely the work of one individual but the culmination of the work of many, for the investigators have, as a rule, used the framework laid by other workers to erect the superstructure. It too frequently happens, however, that we are unaware of much that has been done in related fields so that the application of the discoveries to our own work is for a time completely overlooked.

The investigations of Beaumont (1), London (2), Cannon (3), Cole (4), Forssell (5), and a host of others are of direct interest to roentgenographic practice, and yet in the main they have aroused comparatively little interest among roentgenologists. In the forty years that the opaque meal has been utilized for gastro-intestinal visualization, there has resulted no general recognition of application to roentgen practice of much of the fundamental work which has been contributed by investigators, for even

now there is no standardization of the technique employed in gastro-intestinal investigation. The influence of the consistency of the meal has received scant attention. The even greater effect on the gastro-intestinal tract of the vehicle for the barium has as yet hardly been considered. The divergent practice which results in the use of water, normal saline, buttermilk, malted milk, or whole milk as a vehicle for the barium meal indicates a lack of thoughtful consideration of a very important problem.

If roentgenographic exploration is to keep abreast of the modern advances in the medical sciences it must take cognizance of the results of investigative work which influence roentgenologic practice. This was brought home to us very forcibly a short time ago in regard to the motor meal which is still in use in many departments. In Figure 1-A is shown the gastric emptying and the small intestinal pattern in a normal individual two hours after ingestion of a water-barium meal. In Figure 1-B the water-barium was ingested together with five ounces of black coffee and a slice of toast. The time for gastric emptying was three hours and fifteen minutes. The addition of cream to the coffee, two strips of bacon, and a fried egg resulted in a gastric

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Fig. 1-A.



Fig. 1-B.

Fig. 1-A. Control water-barium meal. Exposure made 2 hours after the ingestion of the meal. The stomach required 3 hours and 5 minutes to empty. The opaque meal entered the cecum in one and one-half hours. Note the distribution and pattern of the opaque meal in the small intestine.

Fig. 1-B. Same individual. The meal consisted of water-barium to which had been added 5 ounces of black coffee and a slice of dry toast. The time of exposure was 2 hours. The stomach required 3 hours 15 minutes to empty. The contents took longer to pass through the small intestine, and did not reach the cecum until three and one-half hours after ingestion of the meal. The distribution of the small intestinal contents is slightly different from that of Figure 1-A. Note the "snowflaky" appearance of the upper jejunum and also that the contents have not entered the cecum as yet.

emptying time of over four hours and fifteen minutes, with a marked change in the small intestinal pattern (Fig. 2). Daily, roentgenologists are reporting gastric retention under similar conditions, with the implication that such findings are of special significance.

It is with the hope of interesting our readers in a more rigid standardization of the technic employed in gastro-intestinal examination, that we are presenting some observations on the gastric emptying time and the small intestinal pattern under a variety of conditions.

The small intestinal pattern in normal individuals must, under the conditions of study with an inert substance such as a water-barium meal, result from the primary preformed folds described by Kerkring and the secondary induced folds of Lesshaft. The small intestine not only plays a major

rôle in preparing foodstuffs for digestion, but it also is the portion of the gastro-intestinal tract which is most active in the absorption of the products of digestion. Forssell (5) believes that during digestion, digestive compartments and digestive alveoli are formed as a consequence of what he has termed the autoplasty of the mucous membrane. A variety of small intestinal patterns may result not only from variations in the muscle tonus, but also in rearrangements of the mucous membrane folds.

Observations which we have previously reported (6) indicate that the small intestinal pattern will vary considerably depending upon the composition of the foodstuff the intestine receives. It varies also with the consistency of the meal, its size, the gastric emptying time, and the tonicities of the intestinal tract. Furthermore, data

have been collected by ourselves and others which indicate that certain pathologic conditions only indirectly affecting the intestinal tract may cause a very profound change in the small intestinal pattern.

The small intestinal pattern is, therefore, subject to many variations from a variety of conditions, and may be assumed to vary depending upon the circumstances imposed upon it at any given period. The realization that such changes may be normal under the conditions of study is of the utmost importance in interpreting the results of roentgenographic exploration.

The Effect of Foodstuffs on the Small Intestinal Pattern.—In the studies which we are reporting, the standard water-barium meal consisted of five ounces of barium and from three to five ounces of water which had been carefully mixed in a mechanical mixer. In the glucose-barium meal 50 per cent glucose was used and in the oil-barium meal olive oil was used. We have reported the exact amounts used in the various meals in a previous paper (6). Suffice it to say that in no instance was the initial consistency of the meal greatly altered from the water-barium mixture. The fluoroscopic observations and roentgen records were made in every instance at



Fig. 2. Same patient as in Figures 1-A and 1-B. Exposure made in 2 hours. The meal consisted of water-barium to which had been added two strips of bacon, one egg, toast, and coffee with cream. The stomach was not empty in four and one-half hours. The contents entered the cecum in 4 hours. Note the marked difference in the small intestinal pattern in this examination to that seen in Figures 1-A and 1-B.

regular intervals so that the effect of varying the vehicle could be studied under standard conditions. The subjects used for these studies were, as far as we were able to determine, normal, healthy young adults.



Fig. 3-A.

Fig. 3-A. Water-barium meal, 41 minutes after ingestion. The "herring-bone" pattern is seen throughout the upper jejunum at A. In the lower jejunum the pattern is more transverse and simulates that of "stacked-coins" at B.

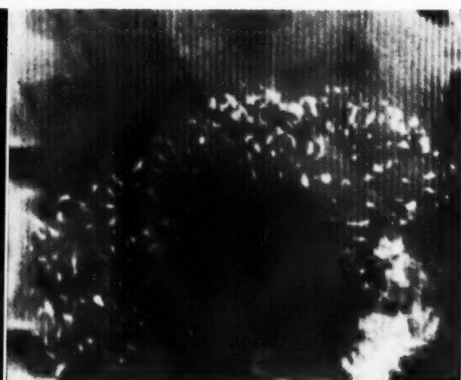


Fig. 3-B.

Fig. 3-B. Water-barium meal, two and one-half hours after ingestion of the meal. The vasa digestiva are visible throughout the upper jejunum as a "snowflake" pattern.



Fig. 4-A.



Fig. 4-B.

Fig. 4-A. Water-barium meal, 24 minutes after ingestion, showing the advance column in the jejunum at A, the segmental contractions at B, and the "herring-bone" pattern at C. There is no central lumen visible.

Fig. 4-B. Same case as shown in Figure 4-A. Water-barium meal, 1 hour 33 minutes after ingestion, showing small irregular boluses in the ileum.

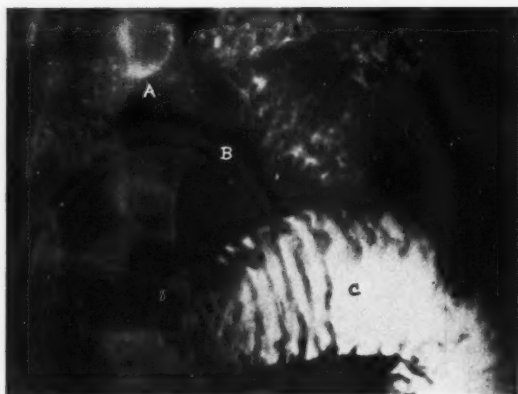


Fig. 5-A.



Fig. 5-B.

Fig. 5-A. Protein-barium meal (raw egg white). The segmental contractions are seen at A, the fine flaky vasa digestiva at B, giving the appearance of iron filings in a magnetic field, and at C there is a large bolus which is occasionally seen in the upper jejunum associated with the pattern of A and B in the protein-barium meal.

Fig. 5-B. Protein-barium meal (egg white). Occasionally the longitudinal folds in the terminal ileum are quite prominent, as seen at A.

Water-barium Meal.—In the majority of instances, the stomach was empty within 2 hours, although occasionally the period was as long as from 2.5 to 3 hours. The small intestinal stream was continuous with little if any regurgitation or peristaltic rushes. In the beginning, the jejunal pat-

tern had a somewhat obscured herring-bone appearance (Fig. 3-A). As the meal passed distally, the herring-bone pattern became more evident and this was followed by a feathery, snowflake pattern, the latter probably being due to retained barium in the vasa digestiva (Fig. 3-B). In the ma-



Fig. 6-A.

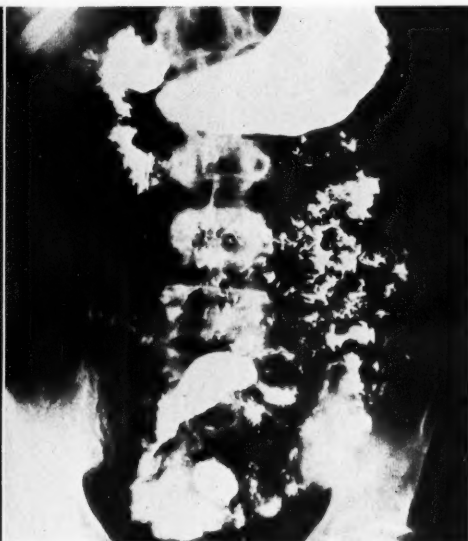


Fig. 6-B.

Fig. 6-A. Glucose-barium meal (50 per cent), showing the contracted pyloric region of the stomach, immediately after the ingestion of the meal. There is a peculiar hypertonic pattern in the duodenum, and in the proximal jejunum there is a homogeneous "cloud" effect which was explained as a dilution effect due to the hypertonic glucose. This is seen only when the hypertonic solution runs right out into the small intestines.

Fig. 6-B. Same case as shown in Figure 6-A, 35 minutes later. Note the coarse, patchy pattern in the jejunum; compare this pattern with that seen in Figure 3-A, which is a control water-barium. Unless one knew that this patient had taken a glucose-barium meal one might be led into making a wrong diagnosis such as changes in the small intestine due to peritoneal irritation.

jority of instances no central lumen was discernible in the jejunum. There was a tendency for the jejunum to have segmental contractions which have been interpreted as being due to circular and possibly longitudinal muscle contractions (Fig. 4-A). In such areas the pattern tended to form longitudinal folds; elsewhere the folds were transverse. Occasionally there was a wavy appearance which was probably due to rapid motility at the moment. In the ileum the pattern was frequently that of a series of small irregular boluses (Fig. 4-B). Occasionally the mucosal pattern was seen and suggested coins placed one upon the other. The intermucosal space was usually wider than that seen in the jejunum. No gas was ever formed in the small intestines of the normal individual.

Protein-barium Meal.—When protein was added to the barium meal there occurred a slight delay in the mean gastric emptying

time. Once the mixture gained entrance into the small intestine, the motility of the observed gut was similar to that seen when the water-barium meal had been taken. In the jejunum there may have been a slight increase in motility and segmental regurgitation. The lumen was slightly less than in the standard meal. There seemed to be more segmental contraction and the pattern was more trabeculated (Fig. 5-A). After the major portion of the meal had passed on, the vasa digestiva were snow-flaky in appearance and quite prominent. One was impressed by the occasional sausage-like bolus, larger than occurs in the jejunum or proximal ileum. The ileum at times tended to show longitudinal folds which could simulate the string sign seen in ileitis (Fig. 5-B). All of these observations were more pronounced when the raw white of egg was used than when the cooked white.

Glucose-barium Meal.—With the glucose-



Fig. 7-A.



Fig. 7-B.

Fig. 7-A. Olive oil-barium meal. Examination made 4 hours after ingestion of the meal; the stomach has scarcely begun to empty. Note the small amount of barium distributed throughout the small intestines.

Fig. 7-B. Olive oil-barium meal. There is a residue in the stomach at the end of 7 hours. The mucosal pattern in the jejunum is obscured. The appearance is that of irregular boluses "smudged" in type.

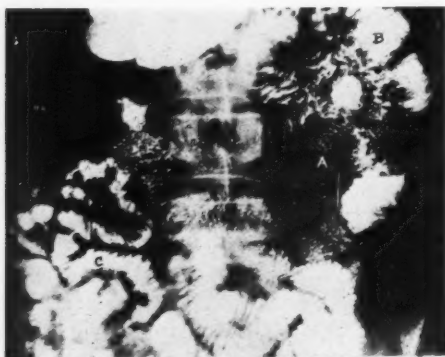


Fig. 8. Magnesium sulphate-barium meal, 45 minutes after the ingestion of the meal, showing the variegated pattern throughout the small intestine. The "snowflake" pattern is seen at A, the obscured "herring-bone" pattern is seen at B, and the "stacked-coin" pattern in the ileum at C. Compare this pattern with the control water-barium meal illustrated in Figure 3-A.

barium mixture the retardation of gastric emptying time was much more marked than with the protein meal. However, once the meal advanced beyond the pylorus it moved with considerable rapidity. Gas-

tric motility began immediately in some cases, and the intestinal stream produced a cloud effect in the jejunum as though the hypertonic solution caused the mucosa to pour out fluid in an attempt to dilute the opaque medium (Fig. 6-A). The motility in the upper jejunum in such cases was very slow, if any. This appearance was followed by a pattern that was coarse and patchy and quite different from the water-barium pattern (Fig. 6-B). The impression one received was that the response might have been the result of mucous membrane irritation with a resulting irregular type of segmental spasm. The pattern was not unlike that seen at times in the presence of an irritative lesion involving the small intestine. After a time, the pattern frequently appeared to be like that with the water-barium meal, while in some instances small boluses of variable sizes could be demonstrated, and the appearance was not unlike that seen in pathologic lesions of the small intestines or in patients who had peritoneal irritation.



Fig. 9-A.



Fig. 9-B.

Fig. 9-A. Mineral oil-barium, 1 hour after ingestion of the meal. The pattern in the proximal jejunum is "herring-bone" in type. In the early portion of the examination the pattern is similar to that seen in the water-barium meal. Note the "smoke-ring" appearance at A.

Fig. 9-B. Same patient as shown in Figure 9-A, examination being made 2 hours 15 minutes after ingestion of the mineral oil-barium meal and one and one-quarter hour after the examination shown in Figure 9-A. The stomach is entirely empty and all of the opaque meal is present in the dilated loops of the jejunum which correspond in position to the second group of small intestinal coils. The progress through the small intestine is very slow and the pattern is obscured. Compare with Figure 7-B.

The pattern in the ileum suggested an increase in tone because of the narrow lumen. The mucosal folds were often longitudinal instead of transverse; at other times, there were large boluses suggesting an appearance seen when the intestinal wall is thickened.

Generally speaking, when the stomach did not empty immediately, the pattern was similar to that described above for the ileum and jejunum except that the cloud effect (homogeneous haze without mucosal pattern) was not noticeable. Occasionally a central canal could be demonstrated.

Olive Oil Meal.—Of all the vehicles which we studied, the vegetable fats provoked the greatest delay in gastric emptying. The addition of a small amount of olive oil might delay the gastric emptying to from three to five hours above the normal. When the oil-barium mixture reached the small intestine it progressed as an intermittent stream with varying sized, segmental pattern or a string of barium boluses (Figs.

7-A and 7-B). The general appearance was smudgy and in some instances might be mistaken for the pattern observed in pancreatic disease and in steatorrhea or Gee's disease. The appearance in the jejunum and ileum was somewhat similar, with the exception that the lumen of the ileum was much wider than that of the jejunum and wider than in the standard meal.

Magnesium Sulphate.—We have had occasion to observe the gastric emptying and small intestinal pattern which resulted after the administration of certain substances which were not foodstuffs. The addition of a small amount of a saturated solution of magnesium sulphate to the barium meal caused a delay in the normal gastric emptying time. The small intestinal pattern was in certain respects similar to that observed in the glucose meal, but it was more flaky in appearance in the jejunum and not so coarse as in the 50 per cent glucose-barium solution (Fig. 8). The coin arrangement of the more distal small intes-



Fig. 10-A.



Fig. 10-B.

Fig. 10-A. Water-barium meal in a patient with thyrotoxicosis of moderate degree. The examination was made 30 minutes after the ingestion of the meal and the head of the column has already reached the cecum at A. The small intestinal pattern in the jejunum is that of a fine "herring-bone" type seen at B. The pattern in the ileum is similar to that of "stacked coins" seen at C. There is a patchy bolus type of pattern seen at D. Compare this pattern with that seen in Figure 1-A.

Fig. 10-B. Water-barium meal in a patient with hyperthyroidism of moderate severity, 1 hour 10 minutes after the ingestion of the meal. Note that the head of the meal is in the sigmoid at A. The stomach is only slightly emptied. The small intestines and colon are hypertonic in type. Note the increased prominence of the haustral markings at B, with the central lumen of the colon.

tine was, as a rule, much more prominent, but occasionally the longitudinal pattern was seen. Passage through the small intestine was extremely rapid and similar to that seen in hyperthyroid disease.

Mineral Oil.—When mineral oil was substituted for olive oil, the gastric emptying time was not slowed (Fig. 9). The appearance of the small intestinal pattern in the early part of the examination approximated that seen with the water-barium meal. The herring-bone and trabeculated patterns were seen in the upper jejunum, and as the contents progressed to the distal jejunum and ileum they assumed varying sized boluses. The boluses in the ileum had a smudged appearance similar to that seen with olive oil. In addition, the pattern had somewhat the effect of smoke-rings. The mineral oil mixture took longer to reach the cecum, but the small intestine emptied more rapidly than with water-barium, and this increased motility was likewise seen in the large bowel (Fig. 9-B). This difference

in behavior between olive oil and mineral oil was to be expected, since chemically and physiologically the action of the two substances is quite different.

THE EFFECT OF CONDITIONS OUTSIDE THE GASTRO-INTESTINAL TRACT ON THE SMALL INTESTINAL PATTERN

Hyperthyroidism.—In the patient of the hyperthyroid group, the pattern and lumen of the small intestine suggested that there was increased intestinal tone and possibly some shortening (Fig. 10-A). Although the gastric emptying was delayed over the normal, the opaque contents reached the cecum in a much shorter period, sometimes in less than twenty minutes, and in shortly over an hour were in the sigmoid. The coils of the small intestine were sometimes placed in a transverse direction. The lumen appeared to have been definitely narrowed and to contain moderately large compartments. In the early portion of the examination, the pattern in the jejunum



Fig. 11-A.

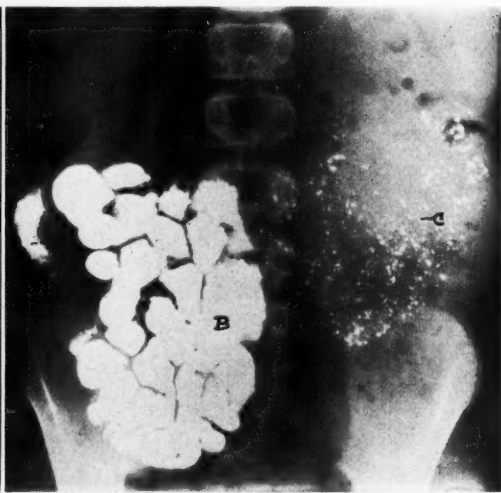


Fig. 11-B.

Fig. 11-A. Water-barium meal in a patient with nephrosis, examination being made 1 hour 16 minutes after ingestion of the meal. The small intestinal pattern is largely obscured and there are a number of small boluses throughout the jejunum and ileum. Compare with Figures 3-A and 10-A.

Fig. 11-B. Examination made 2 hours 45 minutes after ingestion of the meal. The contents have just reached the cecum at A. The small intestinal pattern of the ileum is largely obscured and small boluses are seen at B. There is a "snowflaky" appearance present at C.

was herring-bone in appearance with no definite central lumen. The appearance of the ileum pattern was irregular in the early portion of the examination, and later assumed a stacked coin and bolus pattern. The large bowel was, as a rule, hypertonic (Fig. 10-B).

Nephrosis.—Certain data which we have collected suggested that in the presence of conditions associated with a lowering of the serum proteins, the motility and pattern of the gastro-intestinal tract might be influenced. In nephrosis, the small intestinal motility was decreased. The appearance of the small intestine even after complete gastric emptying suggested large areas of unfilled gut in that a moderately large portion of the bowel was compactly filled with the barium while the remainder of the tract was not visible. At times the picture was not unlike that which might be observed in the photograph of a large bunch of Belgian grapes.

The emptying time of the stomach was normal or slightly delayed. The duodenum was retentive and not spastic. In the up-

per jejunum, the appearance at first was normal, the opaque stream being continuous and the herring-bone pattern predominant. In approximately an hour the small intestinal activity was distinctly abnormal, peristaltic rushes and regurgitation being pronounced and the pattern being a mixture of herring-bone in the proximal jejunum and small boluses in the distal portion. The lumen was slightly less than is regarded as normal (Fig. 11-A).

It required two hours for the contents to reach the ileum; the pattern was short boluses and a small lumen at first, followed by a larger lumen than is usually seen in the normal. There was a distinct delay of the contents in the ileum (11-B).

Diabetes Insipidus.—In diabetes insipidus there occurred a delay in the gastric emptying time. The small intestinal pattern in the early portion of the examination was normal (Fig. 12-A). Later, the pattern became abnormal, in that there was a tendency to form boluses in the jejunum. There was marked delay in motility. The patient from whom these films were ob-



Fig. 12-A.



Fig. 12-B.

Fig. 12-A. Water-barium meal in a patient with diabetes insipidus, before treatment. Examination made 50 minutes after the ingestion of the meal. The contents have progressed very slowly and are still present in the jejunum. The pattern is approximately normal but the loops are quite wide.

Fig. 12-B. Same patient as 12-A, with diabetes insipidus. Examination was made after treatment, and the film was made 1 hour 15 minutes after the ingestion of the meal. Note that the progress of the meal is much more advanced than that found in 12-A.

tained was voiding from 6,000 to 7,000 c.c. of urine per 24 hours. After the daily administration of pitressin for three weeks, the urinary output was reduced to 3,500 c.c. per 24 hours, and at that time the water-barium meal disclosed an increase in the motility of the stomach and small intestine (Fig. 12-B).

Pituitary Tumor.—We had the good fortune to have an opportunity to study the small intestine in patients with pituitary tumor (Fig. 13). The gastric emptying time was considerably increased. The upper jejunum appeared normal for a few minutes, and later the jejunum and ileum presented a striking picture with the greatly reduced size of the small intestinal lumen and rapid motility. The stream reached the ileum rapidly but was delayed there somewhat and the appearance was similar to that seen in some cases of hyperthyroidism.

The Emptying of the Stomach and the

Small Intestinal Pattern of Various Gastric Operations.—We have studied the gastric emptying time under a variety of conditions after simple gastro-enterostomy, pylorotomy with restoration by the Polya technic, and after subtotal gastrectomy. In the first group only was the pyloric sphincter intact, so that gastric contents could leave the stomach by passing either through the new stoma or through the pylorus.

The fact of major interest to us in these patients was that regardless of the type of operation the meal did not pass rapidly through the stomach into the small intestine. Under no circumstances with the water-barium meal which we used did we observe "dumping," although the mean gastric emptying time was somewhat shorter after gastric operation associated with a new stoma.

When a glucose-barium or oil-barium meal was substituted for the water-barium

meal in these same patients, the effect on the gastric emptying time was similar to that of the normal stomach with the pylorus intact. Occasionally, after simple posterior gastro-enterostomy we observed a more rapid emptying time with the glucose-barium meal but this was the exception to the rule.

The intestinal patterns which we observed in these patients were similar to those observed after the same type of meal in a subject whose pylorus and stomach were intact.

Of considerable importance is the knowledge that such a stomach, whose pyloric mechanism has been removed, will function under the conditions daily imposed upon it to a very marked degree as will the normal stomach.

SUMMARY

The variation in the emptying time of the stomach and intestine, and the small intestinal pattern under a variety of conditions which may be imposed on the gastro-intestinal tract by diet, by lesions primarily not involving the gastro-intestinal tract, and by operation, have been presented with the hope that careful observations by the members of this Society may lead to a more accurate and general recognition of the variations which they may cause, even though there is no existing pathologic lesion of the small intestine.

The data which we have presented show clearly that the pattern of the small intestine may vary widely under a variety of conditions. The pattern and motility obtained in normal individuals, with a variation of the vehicle of the barium meal may suggest serious pathologic lesions, and the roentgenologist must be cognizant of the fact that under the conditions of study the appearance may be normal.

These data likewise indicate that there are, in a broad sense, typical reactions of the gastro-intestinal tract with respect to various pathologic entities not associated directly with this tract. Many pathologic conditions yield an intestinal reaction which is grossly characteristic for that dis-

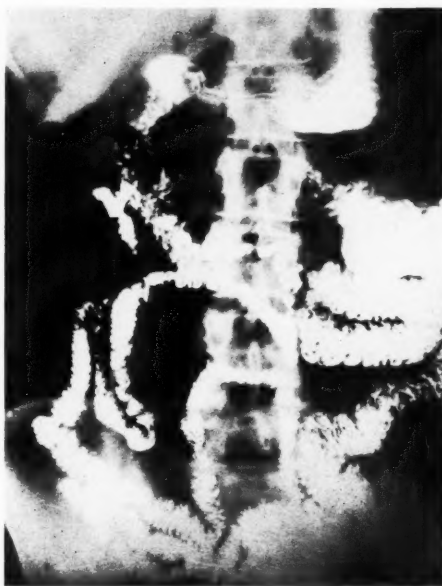


Fig. 13. Water-barium meal in a patient with pituitary tumor, 40 minutes after the ingestion of the meal. The small intestinal pattern is quite hypertonic, especially in the ileum. The segmentation of the small intestine is much more marked in these cases than in the control group. Compare with Figure 1-A.

ease. We have as yet studied only a few disease entities under standard conditions, and it is impossible to state at present whether or not other conditions may simulate the intestinal reactions which we have described.

Only by a fuller understanding of the many processes involved in the mechanism of intestinal motility and of pattern production will we be able to explain the results of studies such as we have presented. The careful roentgen study of the gastro-intestinal tract will add new and important data to the knowledge now at hand on the physiology and pathologic-physiology of this system. In order that the data, whether they be from clinical or laboratory investigations, be suitable for comparison, it is necessary that a standard technic for roentgen exploration be adopted.

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SKELETAL CHANGES IN DISTURBANCES OF THE PARATHYROID GLANDS¹

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INTRODUCTION

KNOWLEDGE as to the function of the parathyroid glands has been built up from observation in several fields. Previous to 1924, the principal physiologic approach was to observe the sequelæ of extirpation of the glands in animals. Since 1924 (9), it has been possible to reverse the situation by the injection of Collip's parathyroid extract (18 and 17). In 1926, Mandl (20) demonstrated that a corresponding hyperparathyroidism occurs spontaneously in patients suffering from parathyroid adenomas, and quite recently it seems to have been established that the same condition may follow simple hyperplasia of these glands (3) under the influence perhaps of an over-production of hormone by the anterior lobe of the pituitary (11 and 15).

Arguing from clinical and laboratory studies on material of this sort, it is now generally believed that hyperparathyroidism, either spontaneous or induced, causes an excessive amount of calcium and phosphate to pass from the bones into the blood, resulting eventually in the generalized skeletal condition known as osteitis fibrosa cystica or von Recklinghausen's disease (24). Removal of an abnormal gland or cessation of extract injection slows up the outward calcium and phosphate tide, following which normal processes, only dimly understood, slowly return calcium phosphate to the bones until calcium ion concentration in the plasma falls to normal levels. There is excellent recent literature covering most of the phases of parathyroid function and dysfunction (2, 5, 8, and 25) and much of this ground has been surveyed in reviews (13, 16, and 30). Sketched in the merest outline, the situation is about as follows:

¹Presented before the Radiological Society of North America, at the Twenty-first Annual Meeting, in Detroit, Dec. 2-6, 1935.

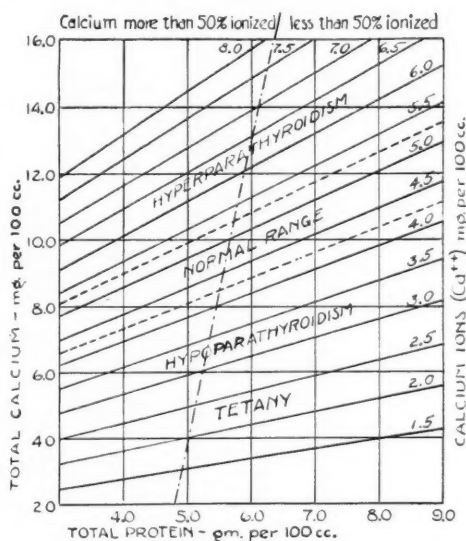


Fig. 1. Chart from McLean and Hastings (21). Total calcium values in excess of 12 mg. per cent are in themselves almost always conclusive evidence of significant elevation in ionized calcium. However, at 10 mg. per cent total calcium, failure to estimate protein as well as calcium might mask a physiologic hypercalcemia if protein were low or hypocalcemia if protein were unusually high.

STATE OF CALCIUM IN THE BLOOD

The circulating plasma of a normal subject contains from 3 to 6 mg. per cent of phosphate (higher in children, lower in adults), 10 mg. per cent of calcium, and about 6.5 grams per cent of protein. At these concentrations, about 5 mg. per cent of the calcium is combined with protein and thus rendered physiologically inert, while about 5 mg. per cent is ionized and therefore free in solution in the plasma and physiologically active (21). (See Fig. 1.) The actual calcium ion concentration at any one time is the resultant of an equilibrium between the total calcium and the total protein present in the plasma.

It is important to the body that the calcium ion concentration of the plasma remain within the physiologic range of from

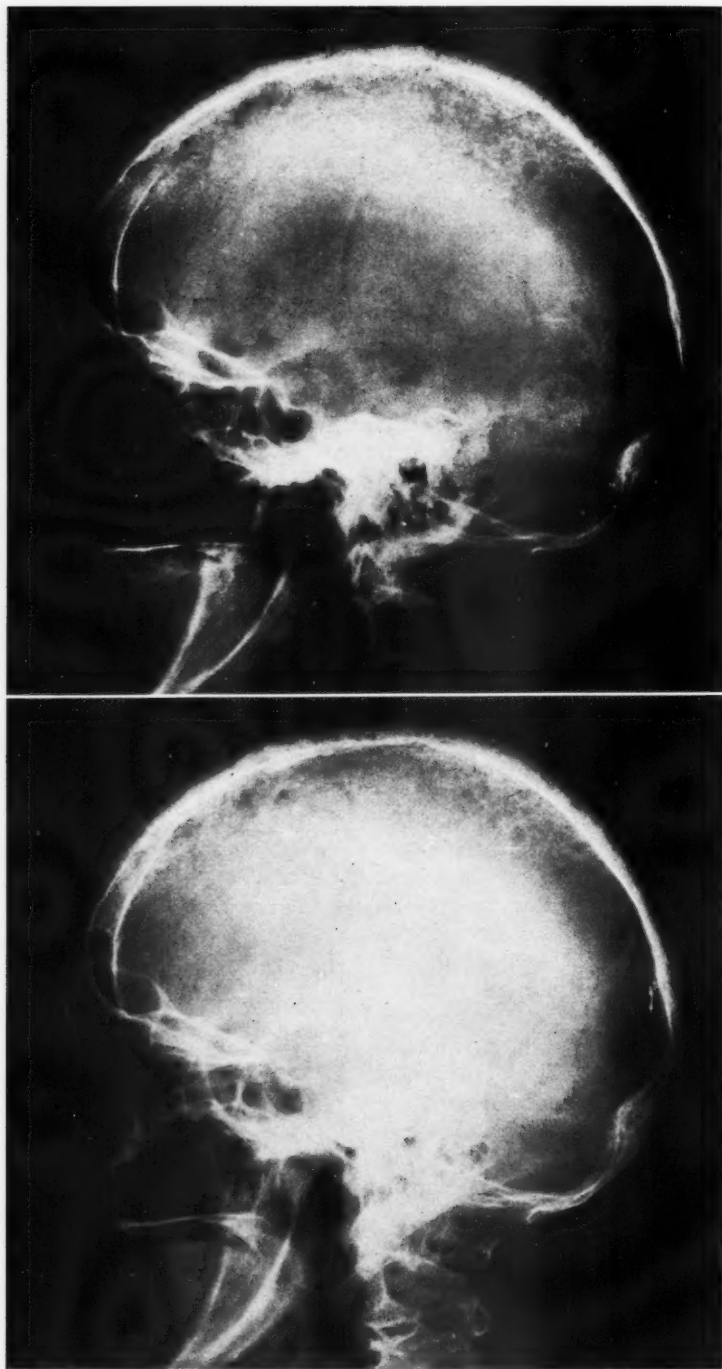


Fig. 2. Osteitis fibrosa generalisata, moderately advanced stage.
(A) (above) L. J., No. 4,850, May 28, 1929. Total serum calcium 12.55 mg. per cent. At operation one month later, D. B. Phemister removed a parathyroid adenoma (10). (See next page.)



Fig. 3. Osteitis fibrosa generalisata, early stage.

(A) (left) E. B., No. 27,621, July 11, 1933. Right shoulder of a 12-year-old girl, who subsequently proved to have parathyroid adenoma. Plasma calcium very high, phosphate low. Note fibrous appearance of humeral shaft owing to deossification of minor trabeculae. Note also slight curvature of shaft resulting from old fracture. Metastatic calcification has occurred at the surface of the acromial epiphysis, a structure which at this age is commonly non-ossified and therefore invisible.

(B) (right) Same case, March 11, 1935. In the normal child, the ossification center for the acromion does not appear until some time between the fifteenth and seventeenth year. Here, at the age of 14 and in the absence of an ossifying center, the acromion has become almost completely calcified by spread from peripheral deposits. At operation, by D. B. Phemister (23), March 16, 1935, a parathyroid adenoma was removed.

4.25 to 5.25 mg. per cent. Below this minimum, excitability of nerve, muscle, and other excitable tissues increases until at very low levels tetany occurs. Above this maximum, nerve excitability falls, metastatic calcification occurs in soft tissues (particularly those that are relatively alkaline, 29), kidney tissue is damaged by the act of eliminating excess calcium and phosphate, and kidney stones may form

because of the high concentration of calcium and phosphate in the urine.

Fluctuations in total calcium of the plasma may occur in response to fluctuations in the concentration of protein. Thus, in multiple myeloma, with high plasma proteins, plasma calcium is high. Conversely, in the case of low plasma proteins in certain forms of nephritis, plasma calcium is low. Such compensatory

(Continued from page 664.)

(B) (below). Same patient, May 7, 1935. Following operation, serum calcium fell and remained down, and, clinically, the patient is greatly improved. Osteoporosis persisted, however, in the skull and other bones.

In both films please note the following: Generalized thickness of skull bones without increase in density, lack of differentiation between cortex and diploë, and small, rounded, particularly translucent areas that may be cysts.



A



B

Fig. 4. Osteitis fibrosa generalisata, early stage (same case as shown in Figs. 3-A and 3-B). (A) frontal view of right knee; (B) lateral view.

Metastatic calcification has occurred at the surfaces of the epiphyseal cartilages of the femur, tibia, and fibula, and these structures have reached a normal size and shape for a child of this age. The diaphyses are unusually slender, however, and their cortex is thin, these findings being in keeping with the idea that an excess of parathyroid hormone speeds up the working-over of bone by osteoclasts, but does not interfere with development of bone from cartilage.

Note also the fibrous appearance of diaphysis, resulting from the persistence of the major trabeculae after the minor trabeculae have been absorbed.

changes in plasma calcium are necessary for the maintenance of normal calcium ion concentrations and are not in themselves of clinical importance.

NORMAL PARATHYROID CONTROL OF CALCIUM

Designed apparently as an essential part of the mechanism for calcium regulation, the parathyroid glands react to rises and falls in calcium ion concentration in the same manner that a delicate thermostat would respond to rises and falls in temperature. When calcium ions fall, more hormone is put out; when they rise, less is produced. Calcium, when bound to protein, produces no effect whatever.

The hormone thus measured out in response to fluctuation in ionized calcium produces no direct chemical effect upon the constituents of the blood plasma and does not increase the chemical solubility of calcium phosphate in plasma (21). It does, however, control the rate at which calcium and phosphate are returned to the blood as a result of the breakdown of old bone.

To those who look upon osteoclasts as connective tissue cells specially differentiated for the absorption of bone, the hormone acts by stimulating these cells, possibly through the mechanism of increasing the acidity of the fluids enclosed by their cell membranes; while to those who con-

sider them merely as scavenging cells, action is upon the tissue fluids in intimate contact with bone but outside the blood stream (16). It is suspected but by no means established that the hormone controls osteoblast activity as well, though possibly the sclerosis (26) that follows long-continued injections of parathyroid extract in animals is to be explained as repair of injury after the establishment of tolerance rather than as evidence of direct osteoblast stimulation.

CALCIUM REGULATION IN HYPERPARATHYROIDISM

In parathyroid adenoma or hyperplasia, an excessive amount of hormone is poured into the blood, and the resulting rise in plasma calcium fails to suppress the further output of hormone or else acts only at abnormally high levels. Total calcium in the plasma may go to 16 mg. per cent or much higher, at which levels it begins to appear in the urine, eventually to the detriment of the kidneys. Large amounts of phosphate are withdrawn from the bones and returned to the blood along with calcium, but presently this is more than offset by a marked increase in phosphate in the urine, so that until kidney damage occurs plasma phosphate is characteristically low.

CALCIUM REGULATION IN HYPOPARATHYROIDISM

Following total removal of normal parathyroids or of normal glands plus adenomas, parathyroid hormone disappears from the blood and the circulatory stimulus to osteoclast activity is lost. As a result, in the absence of local stimuli, such as fractures and infections, osteoclast activity falls to a minimum and there is almost no return of calcium and phosphate from the bones to the blood. Eventually the normal processes that tend to withdraw calcium from the blood bring calcium ion concentration down to a very low level, and unless this is raised by the direct injection of calcium salts, the deliberate increase of

net absorption of calcium from the intestine by appropriate measures, or the injection of parathyroid extract to bring calcium back from the bones, tetany levels are reached and finally death occurs.

Almost nothing has been published as to the x-ray or microscopic findings in the bones of previously normal animals or patients suffering from hypocalcemia due to removal or underfunction of the parathyroid glands. It is known, however, that vigorous calcium medication in normal subjects produces a gradual increase in the density of the skeleton (1), and presumably an equivalent increase in the net absorption of calcium would have an even greater effect in hypoparathyroidism, a condition in which the return of calcium from the bones to the blood is less than normal. It has been suggested but by no means established that Paget's disease and the condition known as marble or chalky bones may be due to underfunctioning of the parathyroids.

There are many reports of cases in which skeletal deossification due to parathyroid adenoma has been followed by reossification after removal of the tumor. Not infrequently, however, though serum calcium returns toward normal and symptoms disappear, there is merely a halting of progressive deossification without demonstrable return of normal bone density (10). (See Fig. 2.) Perhaps in such instances the bones have suffered fibrosis of an unusual type or degree, or possibly there has been failure to push net absorption of calcium from the intestine during the post-operative period.

X-RAY DIAGNOSIS OF SKELETAL LESIONS IN HYPERPARATHYROIDISM

Terminology.—From the first, x-rays have been used in conjunction with microscopic and chemical studies in the laboratory phase of this problem, and in this work there has been little confusion or disagreement. On the clinical side, however, x-ray findings in questionable cases frequently confuse rather than clarify the issue (19), owing in part to a multiplicity



Fig. 5.



Fig. 6.

Fig. 5. Osteitis fibrosa generalisata, moderately advanced stage (same case as shown in Figs. 2-A and 2-B). This film, made Aug. 5, 1930, about one year after the operation, shows "smudged-out" areas at the thinnest parts of both iliac blades. Even in normal subjects, marrow trabeculae are scanty in such thin parts of the bone, so these regions are good places in which to look for early stages of replacement of trabeculae by fibrous tissue.

Fig. 6. Paget's disease of the skull, circumscripta type. G. J. B., No. 14,042. Frank Paget's disease in a male.

Large map-like areas in the anterior two-thirds of the calvarium indicate regions of absorption of old bone. In these translucent regions there are, however, numerous irregular buttons of sclerotic bone. Borders between old bone in the occiput and those areas in which absorption has occurred are sharply differentiated. In this case, serum calcium was not elevated, and biopsy of certain long bones showed the characteristic histology of Paget's disease.

and inexactness of the x-ray diagnostic terms that have been handed down from the days when osteitis fibrosa generalisata was studied principally in its terminal stages as it was seen in the autopsy room. For example, "fibrosa" is a reasonable term to the pathologist because at all stages of the disease he finds an excess of white fibrous tissue laid down among bone trabeculae. To the roentgenologist, however, fibrous tissue is transparent and, therefore, homogeneous and indistinguishable from other soft tissues or fluids except fat, so its presence can be inferred only by alterations it may produce in the calcified portions of trabeculae. The roentgenologist does see a "fibrous" condition of bone at certain stages of hyperparathyroidism, but the "fibers" a recoarsened bone trabeculae, not fibrous tissue (Figs. 3 and 4). Cysts are definite entities to the pathologist, whether they be large or small, located in areas rich in calcified bone or in fields of calcium-free fibrous tissue. To

the roentgenologist they are quite invisible unless they encroach upon calcified trabeculae or cortex, and even then they cannot be distinguished from similar excavations containing fibrous tissue or tumor rather than cystic fluid.

Early Stages.—The primary bone lesion of hyperparathyroidism consists of the vigorous removal of existing marrow trabeculae by osteoclasts, followed by deposition of a field of fibrous tissue in which short, slender, irregular new trabeculae are laid down. In the earliest stages these changes are not shown by the x-ray, but if the process continues roentgenograms begin to show generalized increased translucence of more or less severe degree. This cannot be distinguished directly from the translucence observed in other conditions, such as disuse. Uniformly distributed translucence, particularly in the presence of metastatic soft tissue calcification, may raise suspicion of hyperparathyroidism, and if clinical and chemical examinations insti-

TABLE 1.—CHEMICAL DETERMINATIONS

Disease	Concentration in Blood			Excretion on Low Calcium Diet			
				Urine		Feces	
	Calcium	Phosphorus	Phosphatase	Calcium	Phosphorus	Calcium	Phosphorus
Hyperparathyroidism.....	High	Low	High	High	High	Normal	Normal
Tetany due to parathyroid deficiency.....	Low	High	Very high	Low	Low	Normal	Normal
Osteitis deformans (Paget's disease).....	Normal	Normal	Very high	Very high	Very high	High	High
Osteomalacia from deficiencies.....	Normal or low	Low	High	Low	Low	Low	Low
Rachitis.....	Normal	Normal	Normal or low	Normal	Normal	Normal	Normal
Arthritis (both types).....	Normal	Normal	High	Very high	Very high	High	High
Hyperthyroidism (exophthalmic goiter).....	Normal	Normal	Normal or slightly elevated	Low	High	High	Normal
Steatorrhea difficulty in absorbing calcium from intestinal tract.....	Normal or low	Low					

Clinical findings in blood, urine, and feces in hyperparathyroidism and conditions likely to be confused with that disease. (Adapted by Churchill and Cope from work by J. C. Aub.)

gated by the suspicion prove positive, obviously the radiologist's contribution is of major importance. X-ray evidence of osteoporosis in the absence of clinical and chemical evidence of the disease does not warrant a diagnosis of hyperparathyroidism; on the other hand, absence of osteoporosis does not prove that the disease is not present.

At later stages, when minor trabeculae are largely destroyed but the major trabeculae remain, one may see on the film a coarse "fibrous" pattern, but this may be present also in osteomalacia and rickets, and Todd has reported it as a normal finding in anthropoids and some humans (27).

Stippling of the skull bones has been described as characteristic of early stages of this disease (7) but, as a matter of fact, is not characteristic.

Moderately Advanced Stage.—If the calcium drain continues, bone cortex becomes thin, and in cancellous bone "smudged-out" areas appear (Fig. 5) in regions in which destruction of old trabeculae is complete, and only delicate malformed new trabeculae remain sparsely scattered in fields of transparent fibrous tissue. If the cysts which eventually form are small and largely surrounded by fibrous tissue, they will not be shown by the x-ray, but if they are large and bordered by bone they can be seen.

Almost characteristic of the disease is an appearance of the skull, which has been reported in many cases. Instead of the normal pattern of inner and outer tables with diploë between, one sees in lateral views parietal bones two or three times as thick as normal but made up of translucent, amorphous, homogeneous bone, the diploë being indistinguishable from cortex (Fig. 2).

Advanced Stages.—Far advanced cases are apt to be complicated by areas of absorption due to hemorrhage, large cysts, giant-cell tumors, bowing of long bones, and deformity due to fractures. Unless repair after fracture or osteotomy has produced confusing sclerosis and callus, x-ray findings at this stage are, to say the least, suggestive. Taken together with a history

of long invalidism, they practically assure the diagnosis. Under certain circumstances, however, films made at this stage may mislead the radiologist and cause him to make a diagnosis of Paget's disease.

graphic or microscopic similarity to osteitis fibrosa generalisata. Briefly, in Paget's disease, the x-ray differences are: sclerosis and cortical thickening rather than osteoporosis and cortical thinning; skeletal in-



Fig. 7. Paget's disease: extra-skeletal calcification. L. P., No. 14,510, April 15, 1931. Kidney stones and metastatic calcification (defined as calcification of otherwise normal soft tissue in distinction from calcification occurring as a sequel to necrosis) are such common findings in the hypercalcemia of hyperparathyroidism that their presence should and does raise a suspicion of that disease. On the other hand, kidney stones are not uncommon in Paget's disease; calcification of vessels is almost the rule, and in the case shown here a large uterine myoma is densely crusted with calcium.

Usually, vertebræ are particularly transparent, "fish-shaped," owing to pressure from resilient intervertebral discs, or here and there deformed by compression fractures. All of these findings, however, are consistent with a diagnosis of extensive metastatic osteolytic neoplasm or even multiple myeloma (22).

DIFFERENTIAL DIAGNOSIS

Paget's Disease.—The cause of Paget's disease remains a matter of speculation, and the possibility that it may turn out to be associated with diminished or perverted parathyroid hormone has not been disproved. There is a vast amount of clinical evidence against this view, however, and typical cases show little clinical, radio-

volvement, widespread but almost never complete; skull bones thick but not showing the characteristic amorphous translucence of osteitis fibrosa generalisata. Even in the circumscripta type of Paget's (Fig. 8), the abrupt transition from normal to deossified bone is quite unlike anything seen in osteitis fibrosa generalisata. It must be admitted, however, that atypical cases of either disease may be confusing to the pathologist and roentgenologist. This is evidenced by the older writings of European pathologists, by instances of osteitis fibrosa generalisata in which the skull shows patchy or "woolly" densities (14), and most recently by Kienböck's contention that Mandl's original patient really had Paget's disease rather than oste-

itis fibrosa generalisata (19). The presence or absence of soft tissue calcification or kidney stones is not conclusive because these may be absent in osteitis fibrosa generalisata or present in Paget's disease (Fig. 7). Fortunately, chemical studies of the blood yield quite different values in these two diseases and these findings, together with the whole clinical history, usually establish the diagnosis.

Osteomalacia.—It is questionable whether x-ray examinations alone can ever be depended upon to differentiate between the acute stage of osteitis fibrosa generalisata due to a primary elevation of parathyroid hormone and osteomalacia due to a decreased net absorption of phosphate from the intestine complicated by increased withdrawal of calcium by fetus and lacteal glands. The confusion becomes even worse when in osteomalacia a chronically lowered serum calcium produces secondary parathyroid hyperplasia. However, microscopic examination of bone, chemical examination of the blood, and the clinical history added to the x-ray findings usually make differentiation relatively easy.

Giant-cell Tumors, Bone Cysts, and Regional Fibrosis.—Evidence is scanty as to whether irradiation depresses the activity of normal parathyroids (22 and 28), but there seem to be authentic cases in which irradiation of these glands has benefited bone lesions in proved cases of hyperparathyroidism (12). The subject is important, of course, and is bound to receive increasing attention now that parathyroid hyperplasia seems to have been established as one of the causes of osteitis fibrosa generalisata. We are concerned here merely with the diagnostic implications of the irradiation of the parathyroids.

There are few to-day who believe that local giant-cell tumors or solitary bone cysts are manifestations of increased parathyroid activity. Opinion is much less unanimous, however, in the case of regional fibrosis involving one or at most a few bones, because radiologically and histologically these localized lesions may ap-

pear identical with those seen in generalized osteitis fibrosa. Some speculate that local or regional fibrosis follows local injury of some unknown nature and is not related to parathyroid disturbance. Others have conjectured that there may be such a thing as transient hyperparathyroidism with complete reossification of the skeleton except in restricted areas of particularly severe fibrosis. Reports that local fibrocystic disease as well as giant-cell tumors and cysts may respond to irradiation of the parathyroids (22) are apt to be interpreted as supporting the latter view. It is hard to believe that lesions of this sort really do sclerose and heal as a result of irradiation or surgical removal of the parathyroids. However, even if it can be proved that there is a response of this sort, though it would constitute an important medical discovery, still it would not prove that such lesions are necessarily a local manifestation of parathyroid disease.

It has been shown that large doses of calcium glucinate by mouth sometimes cause sclerosis of osteolytic carcinoma metastases (6), lesions which certainly are not due to a generalized circulatory stimulation of osteoclasts by parathyroid hormone. Here presumably ingested calcium acts directly by increasing the tide of calcium phosphate to all of the bones, and secondarily by depressing the output of parathyroid hormone, thus reducing the general rate of osteoclasts. If a similar depression of osteoclast activity could be accomplished by irradiation of the parathyroids, conceivably this might bring benefit to various types of bone lesions regardless of their nature or origin.

CLOSING REMARKS

"Knowledge of clinical syndromes due to disorders of the endocrine organs has made rapid strides since 1910, and the symptomatology of the endocrine disorders has been extended and made more precise. There has been a tendency, however, to attempt to push the clinical applications of the scientific advances in endocrinology farther than is warranted, and much confusion has arisen both in the profession and among laymen because of failure to distinguish between mere speculation and well-established

facts. Organotherapy and hormonotherapy undoubtedly have an important future, but genuine success in these fields can be assured only by thoughtful, painstaking, rigidly controlled work; progress is only too likely to be retarded and science to be discredited by the rash enthusiast and the credulous ignoramus."

These words, uttered by L. F. Barker (4), were aimed particularly at "unscrupulous vendors of endocrine products" and the "wishful thinking of unskilled practitioners" who use them. Radiologists, however, will not escape similar criticism unless, as they co-operate in the diagnosis and treatment of skeletal lesions of supposed endocrine origin, they proceed thoughtfully, being safeguarded by rigorous controls. Particularly is this true in the case of the parathyroid glands and the bone changes produced by their hormone.

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X-RAY TREATMENT IN HYPERPARATHYROIDISM¹

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THE history of the parathyroid glands dates back to 1855, when they were first described by Remak, but credit for the discovery commonly goes to Sandström, who, in 1880, published a clear description but regarded them as merely aberrant undeveloped fragments of thyroid tissue. In 1858, Schiff, of Geneva, was the first to disprove the then existing theory that thyroid and the so-called aberrant tissue of thyroid (which was parathyroid as described by Remak) was necessary only before birth. He removed the glands from several animals and all of them died. He communicated this fact to the Academy of Medicine in Copenhagen and later on published it, but it made no impression. In his description of the death of the animals, he described what we now understand to be tetany. It was not until 1891 that Gley, Vassale, and Generali established the function of the parathyroids and differentiated the functions of the thyroids and parathyroids.² As early as 1903, Erdheim (1) studied several cases with skeletal changes associated with parathyroidal hyperplasia. In 1901, Askanazy (2) published the first case of parathyroid tumor, found post-mortem in a subject with fibrocystic disease of the bone. In 1925, Hoffheinz published the result of his series of 25 cases of parathyroid tumor, all of them being associated with, or complicated by, osseous changes. However, it was not until 1926 that Mandl did the first parathyroidectomy in a case of osteitis fibrosa cystica with very good results. Mandl (3) also definitely established that it is *hyperfunction*, not *hypofunction*, that causes the osseous changes; this he did by trans-

planting parathyroid tissue, removed from a victim of an accident who was moribund, into the abdominal wall of a patient suffering from osteitis fibrosa cystica, with immediate exacerbation of symptoms and a marked increase in the destruction of the bones. Following this, Mandl noticed in the same patient an enlargement in the left thyroid region. He removed the left lobe of the thyroids and the parathyroids, at the same time removing also the implanted parathyroids. Following the second operation the patient made a rapid and uneventful recovery.

Experimentally, a great deal of work has been done which has established the relation between the parathyroids and the skeletal system. Collip's (4) meritorious work in the production of a specific parathyroid hormone has greatly advanced the knowledge of parathyroid function. Without this hormone, the knowledge of parathyroids would not have reached the highly developed stage it has attained. Jaffe, Bodansky, and Blair (5) were the first to produce, experimentally, evidence establishing the relation between the parathyroids and the skeletal system. Many workers all over the world have corroborated their results. Among these are: Brechot and Pergola (6) in France, and Zagni and Ciaccia (7) in Italy.

Since the epoch-making operation of Mandl, many surgeons all over the world, Hunter (8) in England, Hellström (9) in Scandinavia, Introzzi (10) in Argentine, Oppel (11) in Leningrad, Shkurov (12) in Kharkov, Russia, Giordano (13) in Italy, Ballin and Morse (14) in Detroit, T. G. Schnabel (15), Albright, Aub, and Bauer (16), of the Massachusetts General Hospital, Thomason and Smith (17), and many others in America, have reported excellent results following the removal of the parathyroids in osteitis fibrosa cystica and re-

¹ Presented before the Radiological Society of North America, at the Twenty-first Annual Meeting, at Detroit, Dec. 2-6, 1935.

² See editorial, Jour. Am. Med. Assn., Sept. 23, 1933, 101, 1,003, in which credit is given to Gley, Vassale, and Generali.

lated bone diseases such as osteomalacia, Paget's, hypertrophic arthritides, rheumatic polyarthritides, and even in some cases of renal calculi.

Until 1933, as far as we know, no case of hyperparathyroidism treated with x-ray over the neck had been reported; this, of course, does not mean that cases of hyperparathyroidism have not been treated with x-ray, considering the number of subjects who have been irradiated for one reason or another over the cervical region.

One of us (E. A. M., 18) was the first, in 1933, to report a series of cases of hyperparathyroidism treated with x-ray over the cervical region. In most of the cases very good results were obtained. It was stated: "My interest in hyperparathyroidism was aroused in May, 1931, by the coincidental healing of an extensive and multiple cystic bone lesion in a patient being irradiated over the cervical region for thyrotoxicosis. The rapid relief of pain, and the uninterrupted and progressive regeneration of diseased bone in this case resulted in a review of the literature covering the subject."

Since 1931, we have treated a comparatively large number of cases of hyperparathyroidism. We want to state that in the opinion of many authorities, osteitis fibrosa cystica is only one of the manifestations of parathyroid hyperfunction as evidenced in the skeletal system. Paget's disease, osteomalacia and even multiple myeloma, some of the arthritides, and some kidney concretions fall into this category. Ewing (19) considers giant-cell tumor the end-result of osteitis fibrosa cystica, placing this disease in the group of hyperparathyroidism. Von Recklinghausen (20) in his original contribution, however, describes only osteitis fibrosa cystica generalisata.

One of us (E. A. M.) has stated that: "Pathologic fracture of the ribs, vertebræ, and long bones, in the absence of malignancy, would justify provisional diagnosis of hyperparathyroidism. Indeed, any unexplained cystic bone disease should be considered of parathyroid origin in the opinion of my associates and myself, and the therapeutic test of irradiation over the

cervical region should be used as a confirmatory diagnostic procedure."

The mechanism which controls calcium metabolism is set in motion by the parathyroids. No one can state with certainty, however, that the hyperfunction of the parathyroid must result in hypertrophy of them (21). Nor is it essential that there be an increase in calcium or a decrease in phosphorus in the blood (though this is often the case). However, it is more than likely that some of the synergistic endocrine glands may decrease their function, or some of the antagonistic endocrine glands may increase their function in order to compensate for the hyperactivity of the parathyroids. There are many cases on record in which cystic bone disease has been greatly improved or cured, following parathyroidectomy or irradiation over the parathyroids, in which the blood calcium was not only normal, but was also below normal. Bloom (22) reports such a case, as does also Beam (23). Bodansky and Jaffe (24) in their experimental work state: "We have found in the literature of parathormone therapy instances in which we suspect the presence of hyperparathyroidism, although hypercalcemia was not observed. In view of the reliance that is frequently placed upon hypercalcemia as a sole criterion of hyperparathyroidism, we should be justified in designating hyperparathyroidism without hypercalcemia as crypthyperparathyroidism. This condition is to be recognized by a negative calcium balance and other evidence of hyperparathyroidism in the absence of hypercalcemia." In many cases, however, there is an increase in blood calcium and a decrease in blood phosphorus and an increase in excretion of both in the urine. We must not forget that calcium and phosphorus determination in the blood is not an easy matter, and that the findings depend a good deal on the time of the day the blood is taken, the diet of the patient, his state of rest, and even of his nervous condition. It is essential that the chemist or technician doing the determining be expert in that process, as it is a delicate titration and colorimetric method.

It has now been definitely established that parathyroidectomies have produced unquestionable cures in cystic bone disease and in related osseous changes. The reason for radiation therapy in hyperparathyroidism is precisely the same as that for surgery. The inhibitory effect of radiation therapy on the function of the duct glands (such as the salivary), as well as on the ductless glands (such as the pituitary, ovarian, thyroid, and thymus) has been definitely established, and there is every reason to believe that the hyperfunctioning parathyroids are certainly no exception to this rule.

The operative procedure of a parathyroidectomy is by no means a simple one. The chief operating difficulty is in finding the tumor, and we must not forget that in not all cases is there a tumor present. The location and number of the parathyroids is by no means constant, as was demonstrated by the work of Dr. MacCallum, at Johns Hopkins, and Dr. Lindsay, our own pathologist, at Garfield Memorial Hospital. Bellin and Morse and Hitzrot and Comroe (25) have removed normal glands in hyperparathyroidism with clinical cures. The following is a quotation from Albright *et al.*:

"Before undertaking this operation, a surgeon must be more than 'just a good thyroid surgeon.' He should know the normal and possible aberrant situations of the parathyroid glands. He must be familiar with the reddish-brown color and smooth surface of the parathyroids in contrast to the granular surface of thyroids. He must be able to differentiate the parathyroids from lymph nodes, collections of fetal fat, and thyroid lobules, and he must be prepared to continue to search even if this leads him into the anterior mediastinum."

It is, therefore, clear that the operation is an extremely difficult one and that the mortality, though not as yet established in a large number of cases, is undoubtedly a vital and important factor.

Radiation of the parathyroids is by no means a difficult task. With the present highly standardized methods and accurate measurements, the desired doses can easily be delivered to the parathyroids. To those who are concerned about the possible de-

struction of the parathyroids and thyroids with resultant tetany or myxoedema, assurance is easily given. In the experience of the large radiation therapy institutions throughout the world, where enormous doses of radiation have been given over the neck for malignant condition, tetany and myxoedema were never observed. Coutard, at the Curie Institute of Paris (an outstanding exponent of the practice of giving large doses of radiation over the neck for malignancies of the larynx and hypopharynx), assures us that he has never seen a case of tetany or myxoedema following his treatment. Our own experience agrees with the findings of all these clinics.

In view of the good results obtained by radiation over the cervical region in hyperparathyroidism, and in view of the difficulty of operative procedure, it seems logical to us that in all cases of diagnosed or suspected hyperparathyroidism, x-ray therapy should be given a trial before surgical procedure is undertaken. Irradiation causes no mortality, nor does it preclude surgical intervention should it be considered later. Since the economic factor must be considered nowadays, we must state that x-ray therapy does not require hospitalization and all the expense that goes with it. In many cases the patients can continue with their work.

In a typical case of hyperparathyroidism, the x-ray findings are characteristic, and are best described by Camp and Ochsner (26). They are, in short, a decalcification associated with multiple cystic areas, and a uniform granular mottling, especially in the skull. The cystic areas are most frequently found at the points of most active bone growth, the metaphyses of the long bones. This has been experimentally proven by Jaffe, Bodansky, and Blair, and others. The vertebral bodies show marked decalcification, are flattened, and often show compression fractures.

The clinical syndrome of hyperparathyroidism consists of the following signs and symptoms: pain in the affected bones; increase of serum calcium and a decrease of

serum phosphorus (not a constant finding); decalcification of some bones of the body (a constant characteristic); increased excretion of calcium and phosphorus in the urine; hypotonia of muscles; deposits of calcium in the kidneys, lungs, and even in the gastric mucosa may or may not be present; anemia; loss of appetite; slight temperature. Hyperplasia or hypertrophy of the parathyroids are often present, though not always.

The most annoying and constant signs and symptoms of hyperparathyroidism are the ones first to yield to irradiation therapy. It is interesting and dramatic to note the disappearance of pain over the part affected, in many cases after the first x-ray treatment over the cervical region. The regeneration of diseased bone is usually noted from two to four weeks after the first series of treatments, though it may take two or three series before bone changes are noted. If there has been a disturbance in the blood calcium and blood phosphorus, it returns to normal usually after the first series of treatments, although here again we emphasize the difficulty of obtaining uniformly satisfactory laboratory reports. The general condition of the patient improves markedly after the first series.

Our present technic is as follows: We treat the anterior cervical region, using an area 15×15 centimeters. This extends from just beneath the chin to a little below the sternal notch. We use 220 kv., 20 ma. 0.5 mm. copper, 50 cm. distance. We give 250 r each day for four successive days, then we wait for a period of three weeks and repeat the series. In many cases two or three series are all that are necessary; however, in some cases, four to five series may be necessary. We want to emphasize again that it has been our experience that in all cases the pain, which is the most annoying symptom, decreases or even disappears after the first treatment.

The general condition improves markedly after the first series. Most of our patients who were incapacitated and were not able to walk or even stand when they first came in, were able to walk and do their

work after the first or second series of treatments.

CASE HISTORIES

Case 1. The patient was a white woman, single, aged 34 years. She first came to us for treatment for thyrotoxicosis; she had had a subtotal thyroidectomy on Aug. 14, 1928. Following this operation, she was relieved of her toxic symptoms. Two years later all the symptoms returned and when she came to us for the first time on May 16, 1931, she was admitted in an ambulance. At this time, she had all the cardinal symptoms of thyrotoxicosis. The family history was non-essential. Physical examination revealed an emaciated woman, very nervous and apprehensive. Pulse was 100; weight, 95 pounds. There was a moderate bilateral enlargement of the thyroid glands with a scar at the site of the previous operation. Wassermann was negative. B.M.R., plus 35. Blood, urine, and calcium were not done. As the patient was placed on the table for treatment, we noted that the right leg was semi-flexed and could not be manipulated without excruciating pain in the knee joint. The knee was slightly swollen. Radiographic examination of the right knee showed cyst-like areas of bone destruction involving the distal end of the femur with some periosteal proliferation. Examination of the chest and skull showed no evidence of abnormality. The usual treatment for thyroid was administered and the patient was sent home. On June 6, 1931, three weeks after the first treatment, there was rather noticeable improvement in her condition. There was some gain in weight, less nervousness, and the knee was straight. The striking thing, however, was that the pain in the right knee had completely disappeared. Another treatment was given on June 27 at which time the patient was able to walk in. There was no pain at all in the knee and the woman was feeling generally well. Radiographic examination of the knee at that time showed marked regeneration of the bone in the cystic areas previously reported. From then on the patient began

to gain in weight. On Aug. 29, 1931, while some of the toxic symptoms of the thyroid still persisted, parathyroid symptoms had completely cleared up and the patient was ready to return to work. She then weighed 140 pounds, and is well to this date and working.

Case 2. The patient, a boy aged 6 years, was admitted to the Children's Hospital Clinic, in October, 1932. He had cut his left heel on a piece of glass, which healed without any complications. A month later he struck his heel and a slight swelling developed. There was no evidence of skin damage or ecchymosis, but the heel was swollen and tender. The clinical impression was osteomyelitis. The leukocytes were 6,700, increasing a week later to 10,000; the temperature, pulse, and respiration were normal. The foot was placed in a plaster cast. Roentgen examination on Jan. 24, 1933, three months after the onset of symptoms, showed an extensive decalcification of the bones of the left foot and a definite area of destruction in the posterior and inferior portion of the os calcis which was thought to be inflammatory. At the request of Dr. John Allan Talbot, who suspected that the disease might be hyperparathyroidism, the child received three treatments over the cervical region at monthly intervals. The pain was entirely relieved following the first x-ray treatment, and the cystic area in the os calcis had healed by May, 1933. The blood calcium in this case was 8.9 mg. per 100 c.c. at the beginning of treatment.

Case 3. The patient was a white woman, aged 62 years. She had fractured her right hip in 1927; complete union followed. In September, 1930, she fractured the right hip at the same site, and cystic areas were noted in the proximal third of the right femur; there was no union. In the late fall of 1932, she developed pain in the right shoulder, right hip, and lower back and became bedridden with intense pain. Roentgen examination disclosed cystic changes in the femora, pelvis, lumbar vertebrae, and the right clavicle. The diagnosis made at that time was hyperparathyroidism, pro-

ducing osteitis fibrosa cystica. Roentgen therapy was not instituted, however, until May, 1933. Five series of treatments over the cervical region were given at intervals of three weeks. The pain has been completely relieved and the general health much improved. The previously bedridden patient is now up and about. There is definite regeneration of the cystic areas, and a bony union between the femur and ilium is being established.

Case 4. The patient was a white man, aged 60 years, whose history was unessential until March, 1929, when he began having pain along the left tendo achillis. This was followed by pain and tenderness in both hands, forearms, and shoulders. The blood calcium at this time was 12.8 mg. per 100 c.c. of blood. In November, 1929, the patient was "seriously crippled" and consulted Dr. Joel E. Goldthwait, of Boston, who found chronic arthritis with decalcification of the bones. He returned to his home in Washington and consulted Dr. Arthur C. Christie on Nov. 29, 1932, who made a diagnosis of hyperparathyroidism, based on the presence of cystic areas in the lower ends of the left radius and ulna, and severe pain. The blood calcium was 12.6 mg. and the blood phosphorus 1.96 mg. per 100 c.c. of blood. Three series were given over the cervical region at intervals of three weeks. There was slight improvement in the cystic areas in the radius and ulna and a diminution in the pain following the second treatment. By June 29, 1933, the patient was clinically well. The blood studies at that time showed 9.03 mg. of calcium and 4.0 mg. of phosphorus per 100 c.c. of blood. An insufficient time has elapsed to show complete healing in the cystic areas.

Case 5. A white woman, aged 70 years, consulted us on Oct. 28, 1932. The past history was of no importance until April, 1932, when the patient developed pain in the lower back and lower extremities. The pain became progressively more severe and gradually extended over the entire back. She was unable to walk and suffered intensely even in the recumbent position.

Roentgenograms of the spine showed extensive decalcification and compression of the bodies of all of the lumbar vertebrae and most of the dorsal. Roentgen therapy was applied, two series being given over the cervical region at intervals of three weeks. There was marked diminution in the intensity of the pain following the first treatment, and the patient was free of pain following the third treatment. On June 6, 1933, eight months after the first treatment, the patient was very comfortable and was able to be up and attend to her usual duties.

Case 6. The patient was a white woman, aged 57 years, who complained of severe pain in the right buttock, small of the back, and right groin, radiating down to the right leg. There was weakness, loss of appetite, and general malaise. The patient had been well until March, 1935, at which time she first noticed pain in the right groin extending to the posterior pelvis and occasionally down the right leg. Since May 1, 1935, she has been bedridden most of the time. The pain seems to be worse on the least bit of motion, and when lying still the pain is intermittent in character. X-ray examination of the pelvis showed extensive changes in the right innominate bone and the region of the acetabulum which has the appearance of a metastatic malignancy. The only other possibilities are myeloma or parathyroid disease. The patient was examined most carefully. Breast, pelvic, and rectal examinations were done and no evidence of abnormality was found. Examination of the urinary tract, intravenous method, gall bladder, gastro-intestinal tract, skull, and chest were negative. Because of all the negative findings for the site of the primary malignancy, it was believed that the disease may represent parathyroid dysfunction, and x-ray therapy was advised. The first series given was started on August 8 and after the first two treatments the patient stated that her pain was considerably relieved. On September 4 the woman returned, feeling much better in general. She was able to sit up in a chair and to walk a little without pain. At this time x-ray

re-examination of the pelvis was made and there was found increased destruction of the areas previously noted. Due to the general improvement, however, and to the disappearance of pain, another series was given. The patient returned eight days later, this time feeling much better in every respect. There was an increase in appetite, pain was entirely gone, and she was able to walk about. Nevertheless, a third series was given and on November 5 the patient returned feeling almost entirely well. She is now able to walk and has no pain at all. X-ray examination of the pelvis and hips at this time shows a very definite increase in the calcification of the areas previously noted.

Case 7. The patient was a white woman, aged 63 years. Previous history was non-essential. In May, 1933, the patient had severe pain in the pelvis and femora; in June, 1933, she was bedridden, with excruciating pain. There was loss of appetite and general malaise. X-ray examination of the chest, dorso-lumbar spine, and pelvis showed narrowing of some of the bodies of the vertebrae, with extensive cystic degeneration. The ribs and bones of the pelvis also showed marked cystic degeneration. There was a spontaneous fracture of the clavicle. Therapy was instituted, three series being given. While changes in the osseous system were not marked, the symptoms of the disease disappeared almost entirely. The patient is now up and about, doing her housework.

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REVIEW OF THE EARLY SCIENTIFIC ASPECTS OF PITUITARY HORMONES AND THE SIGNIFICANT FACTS IN REGARD TO THEIR INFLUENCE ON BONE GROWTH¹

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THE recent advances in endocrinology have been so great that there is hardly a medical specialty that it does not touch and influence to a greater or lesser degree. Hence, I feel that as an endocrinologist I have to make no apologies for appearing before you to-day. I was asked to give you a short address on the physiology of the pituitary gland, but I felt that a paper by my colleague, Dr. Hector Mortimer,² to which I might say a few words by way of an historical introduction, would be of more value to the members of your Society.

Dr. Mortimer has been able to prove that hormones affect bone growth. The idea is not new, but Dr. Mortimer's observations will, I think, give conclusive evidence of the profound effects of certain hormones on skeletal development, differentiation, and architecture.

Before speaking of hormones in particular, let me call to your mind the older observations on the profound effect at times of environmental conditions on the bony structures. Most important of these factors is probably diet in the broadest sense.

I shall now give you a few examples of the manner in which certain hormones may influence the skeleton either directly or indirectly.

In 1924, I showed that parathyroid gland extracts containing the active principle had the power, when injected into dogs, of mobilizing calcium into the blood. Later work established that this calcium came from the skeleton. Calcium metabolism may be influenced by many factors, such as mineral salts and vitamins, pH of body fluids, hormones, etc., but the parathyroid glands must be looked upon as the chief

regulator of calcium metabolism. Since bone and teeth are largely constituted of calcium salts, the importance of the parathyroid apparatus in relation to the development and maintenance of these structures is obvious. Laboratory studies designed to demonstrate the effects of the parathyroid hormone showed very clearly that the calcium salts of bone must be considered as mobile and not fixed. The interchange between the depots in bone and the body fluids of calcium salts may indeed be quite considerable, and an imbalance in this interchange may lead to osteoporosis or osteitis fibrosa cystica, on the one hand, or to marble-bone and allied conditions on the other. It is in this connection that Dr. Mortimer's work is so important, because it helps to explain just what has gone wrong in the normal physiologic processes when certain definite abnormalities in skeletal development or architecture are met with in clinical practice.

The thyroid gland also has a definite influence on calcium metabolism. Thyroid feeding is known to cause a great increase in calcium excretion by the bowel, which results in a negative calcium balance. The increased calcium excretion which results when parathyroid hormone is administered is by way of the kidney. The thyroid hormone does not affect the blood calcium level appreciably, but the skeletal structures give up calcium under either thyroid or parathyroid medication. Animal experimentation has shown that the long continued use of parathyroid hormone results in a reversal of its effect on bone; marble-bone may be formed in the second stage, whereas a condition simulating osteitis fibrosa cystica may be demonstrated when the hormone has been given for short periods. Thus we see that the whole affair is extremely complicated.

The hormones of the anterior pituitary

¹ Presented before the Radiological Society of North America, at the Twenty-first Annual Meeting, in Detroit, Dec. 2-6, 1935.

² Dr. Mortimer's paper has not been received for publication. The Editor hopes to have it for a later issue.

have variable effects upon calcium metabolism. Thus, hypophysectomy results in failure of bone growth. As you well know, the anterior lobe has many active principles and many functions to serve, and an analysis of these indicate that the effects of one active principle may be antagonistic, as regards some special physiologic reaction, to another principle from the same gland. This is well illustrated by an apparent antagonism between the growth or somatotrophic hormone and the thyreotropic principle. Injections of the thyreotropic substance for short periods result in the production of a state of hyperthyroidism. Dr. Leonard Pugsley has been able to demonstrate an increased excretion of calcium in the hypophysectomized rat treated with the thyreotropic hormone. The purified growth hormone has been shown to cause growth of both skeletal and muscular tissues in the hypophysectomized animal. The growth of the skeleton naturally re-

sults in the deposition of calcium, and an actual increase in calcium balance has been demonstrated under these conditions. As regards calcium metabolism, therefore, these two pituitary principles seem to have antagonistic effects.

There is a tendency, which comes as a result of studying the physiologic effects of individual hormone substances, to overlook the integrative action of the whole endocrine system. Perhaps, in the case of calcium metabolism in the widest sense, the integrative action of the endocrines is as well demonstrated as in any other instance.

The paper which Dr. Mortimer will now present, and to which my brief remarks have been only a preamble, will demonstrate, I trust, to your delight as radiologists, the new use to which a highly specialized technic in radiology has been put with a view to elucidating some of the problems which are presented by a study of the hormones.

A STUDY OF A SERIES OF MENOPAUSAL CASES AFTER IRRADIATION OF THE PITUITARY GLAND¹

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THE climacteric, whether natural or artificial, in a large proportion of women produces a series of disturbing symptoms that at times assume distressing proportions. It is generally believed that these symptoms are due to a lack of ovarian secretion, a conclusion substantiated by the sudden appearance of the menopausal syndrome following castration by surgery or irradiation and the relief obtained in many of these cases by the injection of the female sex hormone. However, it is the authors' belief that hyperfunction of the pituitary gland initiated by removal of the ovarian secretion is wholly or in the major part responsible for the appearance of this syndrome. No claim to priority in this view is taken, but pathologic, biologic, and physiologic studies will be presented to substantiate this view, as well as the rationale of irradiation of the pituitary gland for this condition.

Following castration, Tandler and Grosz (1) showed that there is an increase in size and function of the anterior portion of the hypophysis. Rossle (2) found typical "castration cells" appearing in the anterior portion of the hypophysis following castration, and state that these cells may appear as early as four or five days following gonectomy. Evidence that a physiologic as well as a pathologic change occurs was produced by Engle (3) and Evans and Simpson (4), who implanted pituitary tissue from castrated rats into immature animals and showed them to be more potent in stimulating the ovaries than pituitary gland tissue from normal rats. Fluhmann (5) elicited the same results by injecting blood serum from castrated humans but could not do so by injecting blood

serum from women with normal menstrual periods, irrespective of the time of the period the blood was obtained. From their experiments, Nelson (6), Wolfe (7), and Meyer, Leonard, Hisaw, and Martin (8) conclude that the injection of the female sex hormone into castrated experimental animals decreases the amount of gonad-stimulating complex of the hypophysis, with an almost complete disappearance of the so-called "castration cells." These latter experiments prove that the female sex hormone has an inhibitory action upon the anterior hypophysis, and that the results gained by injection of the female sex hormone in the menopause are obtained in this manner.

Newell and Pettit (9) irradiated the pituitary gland for dysmenorrhea, and Fluhmann (cited by them) assayed the blood for anterior pituitary hormone. They concluded as follows: "An abnormal amount of anterior pituitary sex hormone in the blood was apparently reduced by irradiation of the pituitary." From these excellent pathologic, physiologic, biologic, and clinical experiments, the logical conclusion is that the menopause syndrome is due primarily to an abnormal amount of prolactin secreted by a hyperfunctioning anterior lobe of the pituitary, which is initiated by the withdrawal of the follicular hormone of the ovary. Borak (10) states: "A hyperfunction of the pituitary in the menopause, which Holzknecht and I suggested in 1924 on the basis of the effect of radiating the pituitary in climacteric upsets, has been established as a definite field for radiotherapy by the demonstration of an excessive secretion of a follicle maturing hormone by the pituitary after cessation of ovarian function in the menopause."

Previous reports have recently been

¹ Presented before the Radiological Society of North America, at the Twenty-first Annual Meeting, at Detroit, Dec. 2-6, 1935.

published concerning certain favorable results obtained when the pituitary gland has been subjected to irradiation therapy. This form of therapy has been used for some time; in fact, it dates back some twenty-five years when Gramegna and Bécère, in 1909, treated pituitary tumors by irradiation therapy. Shortly thereafter it was observed by certain investigators that patients treated for pituitary tumors with irradiation, who also had certain gynecologic disorders, were relieved of their menopausal symptoms. Hofbauer and Groedel, in 1922, Werner and Sahler, in 1923, and Borak, in 1924, were among the first to use irradiation therapy of the pituitary gland for this purpose.

Failure to obtain desired results with the use of the female sex hormone in some cases of climacteric symptoms stimulated us to try irradiation of the pituitary. The results were so striking that we decided to use this therapeutic measure in all cases of menopausal syndrome encountered in the clinic so that a proper evaluation of its efficacy could be reached.

ROENTGEN TECHNIC

Roentgen-ray treatments were given with 120 kvp., 5 ma., 0.25 mm. Cu, and 1 mm. Al, 30 cm. distance, 8 min., with a small portal given with a cone. The first exposure was given through the right temporal region, and on the following day was repeated on the left side. This constituted a series, each side receiving 148 r measured with back-scattering, making a total of 296 r for both sides, the pituitary gland receiving approximately 104 r. After an interval of about three weeks, the same procedure was again followed, making a total of two series, the skin receiving a total of 592 r, and the pituitary gland receiving a total of about 208 r. While we appreciate that the roentgen-ray dose used in our series of cases was small, in fact, much less than that used by other investigators, we had in mind to use a non-destructive dose, yet one which would produce an ameliorating effect

on the symptoms of our gynecologic patients. Much larger doses could be used without producing any ill effect on the surrounding brain structures, which is capable of tolerating a very large dose of roentgen ray. In this regard, Borak (10) states that he has carried out thousands of irradiations of the pituitary gland in hundreds of cases during a period of ten years without encountering any evidence of injury. We felt, however, that we should feel our way cautiously, especially since small doses were producing satisfactory results. In the future, we are planning to change our technic from time to time, observing whether it will be productive of better results. It may be of interest to mention that Newell and Pettit (9) in a recent publication state that in their series of reported cases they used roentgen ray to the pituitary gland in doses of 385 r (measured in air), directed to each temple, over a period of five weeks, thereby treating various gynecologic disorders with very good results.

At present, we have irradiated a total of 47 cases of menopausal syndrome. Of these, 24 had an artificial menopause, while in 23 it was spontaneous. These cases presented symptoms of flushes, dizziness, sweating, headaches, and nervousness, usually three or four of the symptoms appearing in combination. In a number of patients, the dizziness was so marked as to cause the patients to fall, a few being afraid to venture into the street alone. The flushes varied in frequency; in some patients, they occurred two or three times daily, in others, from ten to twelve times daily, being accompanied by profuse perspiration. Nervousness was a marked feature in the majority of cases. Headaches were least frequent but most difficult to control. Of the 47 cases, 40, or 85 per cent, experienced excellent results, in that all of the symptoms complained of either disappeared completely or occurred so infrequently and mildly as to cause no discomfort or inconvenience whatsoever. In four cases (9 per cent) the results were fair in that, although most of the disagreeable symptoms disappeared, one symptom, usu-

ally the headache, would persist despite treatment. It is our intention to re-radiate these cases. In three cases (6 per cent) the treatment did not produce any improvement whatsoever and here again re-radiation will be tried. Our longest follow-up on any case was 16 months, this patient having remained entirely free of symptoms for this period of time. In several cases, three series instead of two were given because of a return of one of the symptoms in a moderate degree of severity (two cases), or because we wished to determine the effect of a larger dose. In all seven cases, the final result was excellent. It is our intention in the future to give each patient three series of irradiation treatment, and determine if our results can be bettered in this manner. Five of the cases had had injections of the female sex hormone with no result. Following irradiation of the pituitary gland, all these cases showed a marked degree of improvement.

These results compare favorably to those reported by Borak, who, in 1929, reviewed a series of 274 patients, 80 per cent of whom had been so treated with relief; some had been observed for six years. In the remaining cases, some improvement followed subsequent irradiation of the thyroid. Borak attributes this to the fact that the anterior pituitary following the menopause also secretes an excess of thyreotropin hor-

none. We have not resorted to irradiation of the thyroid in any of our cases.

CONCLUSIONS

(1) The menopausal syndrome is primarily the result of an excess of prolactin secreted by the anterior hypophysis initiated by the withdrawal of the ovarian hormone.

(2) Irradiation of the hypophysis for climacteric symptoms produces excellent results in the majority of cases.

(3) Irradiation of the pituitary in the dosage given will not produce any harmful results.

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THE IMPORTANCE OF ROENTGENOGRAPHIC STUDIES OF OSSEOUS DEVELOPMENT IN ENDOCRINE DIAGNOSIS¹

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THE discovery of the x-ray in 1895 provided a means for adequate study of osseous development. Although some confusion is apparent as to what actually constitutes a normal subject, roentgenologists have succeeded in demonstrating with considerable accuracy not only the average time at which the various centers of ossification make their appearance, but, of equal importance, the average age when the epiphyses unite. Furthermore, it has been established, largely through endocrinologic investigations, that definite alterations in the osseous age of an individual result, almost uniformly, from disturbances in function of certain ductless glands. As a result, roentgenographic studies of children and young adults from birth up to 25 years of age may reveal a wealth of information of vast importance in endocrine diagnosis.

Engelbach and McMahon (1) especially emphasized the importance of bone-age studies in the accurate diagnosis of ductless gland disease. In 1924, they summarized the accumulated knowledge of the chronologic appearance of the ossification centers in normal children. Later, the researches of Shelton (2) resulted in the preparation of the tables for normal osseous development (Tables I-IV) which at present are used as standards for determining the skeletal age of both normal and abnormal children.

Although the size, shape, and consistency of the bony framework of the body may be materially altered by hormonal changes which have their beginning in the latter decades, it is obvious that diseases of the

ductless glands originating in adult life can have no influence on skeletal growth. No endocrine affliction having its onset



Fig. 1. Typical case of juvenile myxedema. Age, 12 years 3 months; height, 30 inches; weight, 29 pounds; x-ray bone age, 6 months to one year. (Through the courtesy of Dr. C. Kelly Canelo, San José, California.)

after the twenty-fifth year can unsettle these structural foundations. When, however, the endocrinopathies of infancy, childhood, and adolescence are under consideration, profound influences upon osseous development may be apparent. In fact, radiologic evidence of variation from the accepted normal somatic growth at times assumes a more important rôle in proper diagnosis than do determinations of the basal metabolic rate, studies of the blood chemistry, or other so-called specific laboratory procedures.

Endocrinologists have long been concerned with the hormonal cause of abnormal ossification. For the most part, however, their interest has centered about

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TABLE I.—ROENTGENOGRAPHIC STUDIES IN NORMAL OSSEOUS DEVELOPMENT—INFANTILE
(1-5 YEARS)

Age	Joint	Osseous Centers Present	Time of Appearance According to							
			Engelbach	Baetjer	Knox	Rotch	Poland	Cohn	Allen	
Birth	Knee (Lat.)	*Dist. ep. femur.....	Birth	Birth	Birth	Birth	2d week	Birth	Birth	
		*Prox. ep. tibia.....	Birth	Birth	Birth	Birth	2d week	Birth	Birth	
	Ankle (Lat.)	*Talus, cuboid.....	Birth	Birth	Birth	Birth	Birth	Birth	Birth	
*Calcaneus.....		Birth	Birth	Birth	Birth	Birth	Birth	Birth		
1 year (12 mo.)	Wrist (AP)	*Capitate.....	4th mo.	1st yr.	1st yr.	1st yr.	8th mo.	6th mo.	3-6 mo.	
		*Hamate.....	5th mo.	1st yr.	1st yr.	1st yr.	1st yr.	6th mo.	5-12 mo.	
		*Dist. ep. radius.....	6-8 mo.	2d yr.	2d yr.	2-4 yr.	2d yr.	6th mo.	8-15 mo.	
	Shoulder (AP)	*Ep. head humerus.....	3-5 mo.	6-7 mo.	5th mo.	7th wk.		7th wk.	1-2 yr.	
	Hip (AP)	*Ep. head femur.....	9-11 mo.	1st yr.	1st yr.	1st yr.	10th mo.	6-12 mo.	1st yr.	
		Talus, cuboid Calcaneus								
2 years (24 mo.)	Ankle (Lat)	*Ext. cuneiform.....	1st yr.	1st yr.	1st yr.			1st yr.		
		*Dist. ep. tibia.....	1st yr.	1st yr.	Birth		18th mo.	5th mo.	1-2 yr.	
	Shoulder (AP)	Ep. head humerus								
	Elbow (AP)	*Cr. tub. humerus.....	2d yr.	3-4 yr.	3d yr.	2-3 yr.		2d yr.	2-3 yr.	
		*Cap. humerus.....	2d yr.	1st yr.	2d yr.			17th mo.	2-3 yr.	
		Talus, cuboid Calcaneus								
3 years (36 mo.)	Ankle (Lat)	Ext. cuneiform Dist. ep. tibia								
		*Dist. ep. fibula.....	2d yr.	2d yr.	2d yr.	2-3 yr.	2d yr.	13th mo.	2d yr.	
	Wrist (AP)	Capitate, hamate Dist. ep. radius								
		*Triangularis.....	3d yr.	3d yr.	3d yr.	2-3 yr.	3d yr.	3d yr.	2-3 yr.	
		*Ep. phalanges.....	3d yr.	3d yr.	3d yr.	2-3 yr.	3d yr.	2-3 yr.	1-3 yr.	
		*Ep. metacarpals.....	3d yr.	3d yr.	3d yr.	2-3 yr.	3d yr.	2-3 yr.	3d yr.	
4 years (48 mo.)	Ankle (AP)	Talus, cuboid Calcaneus								
		Ext. cuneiform Dist. ep. tibia Dist. ep. fibula								
		*Ep. metatarsals.....	3d yr.	3-7 yr.	3d yr.	3d yr.		3 yr. 6 mo.		
		*Int. cuneiform.....	3d yr.	3d yr.	3d yr.	3d yr.		3 yr. 6 mo.	2-3 yr.	
	Wrist (AP)	Capitate, hamate Dist. ep. radius Triangularis Ep. phalanges Ep. metacarpals								
	Hip (AP)	*Lunate.....	4th yr.	4th yr.	4th yr.	4-5 yr.	4 yr. 6 mo.	4th yr.	3-4 yr.	
5 years (60 mo.)	Knee (Lat)	Ep. head femur.....	4th yr.	4th yr.	4th yr.		4th yr.	4th yr.	3-4 yr.	
		*Ep. gr. trochanter.....								
		Dist. ep. femur Prox. ep. tibia								
		*Prox. ep. fibula.....	4th yr.	3-4 yr.	4th yr.	4th yr.		4-5 yr.	3-5 yr.	
	Ankle (Lat)	Talus, cuboid Calcaneus								
		Ext. cuneiform Dist. ep. tibia Dist. ep. fibula Ep. metatarsals Int. cuneiform								
5 years (60 mo.)	Wrist (AP)	*Mid. cuneiform.....	4th yr.	4th yr.	4th yr.	4th yr.		3-4 yr.	3-4 yr.	
		*Navicular.....	4th yr.	4th yr.	4th yr.	4th yr.		3-4 yr.	4-5 yr.	
		Capitate, hamate Dist. ep. radius Triangularis Ep. phalanges Ep. metacarpals Lunate								
		*Trapezium.....	5th yr.	5th yr.	5th yr.	5th yr.	4 yr. 6 mo.	5-6 yr.	4-5 yr.	
		*Scaphoid.....	5th yr.	5th yr.	5th yr.	5-6 yr.	5th yr.	4-5 yr.	4-5 yr.	
	Elbow (AP)	Cap. humerus								
Knee (Lat)	*Prox. ep. radius.....	5th yr.	5th yr.	5th yr.	5th yr.		5-7 yr.	4-5 yr.		
	Dist. ep. femur Prox. ep. tibia Prox. ep. fibula									
		*Patella.....	5th yr.	3-4 yr.	3d yr.	2-3 yr.		5th yr.	3-5 yr.	

Osseous centers new to the age are denoted by an asterisk. "Lat." lateral view; "AP" anteroposterior view.

Table showing normal osseous development. Age of patients from birth to 20 years. Taken from the article by Shelton, 1931.

the explanation of a retarded unfolding of the osseous system. Relatively few cases of advanced skeletal development have

a delayed rate of ossification may result not only from disturbances in function of the endocrine system but from other

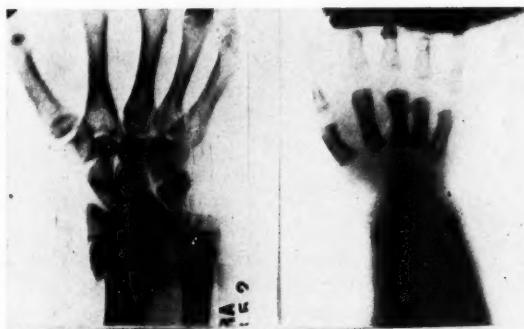


Fig. 2. Retarded bone age characteristic of juvenile myxedema. *Left:* Normal child—chronological age, 12 years; x-ray bone age, 12 years. Note all carpal bones present. *Right:* Childhood myxedema—chronological age, 12 years 2 months; x-ray bone age, 6 months to 1 year. Note only two carpal bones present. (Through the courtesy of Dr. C. Kelly Canelo, San José, California.)

been reported, although the finding of an accelerated bone age is equally as important clinically as is the demonstration of a retarded bone age; in fact, it may be more so. Normal bony development predicates normal body metabolism. Consequently,

factors, usually dietetic in nature, which profoundly affect the rate of general body metabolism. One has only to recall the retarded growth and physical development of the diabetic child during the pre-insulin era to realize the effect of an inadequate

TABLE II.—ROENTGENOGRAPHIC STUDIES IN NORMAL OSSEOUS DEVELOPMENT—JUVENILE (6-12 YEARS)

Age	Joint	Additional Osseous Centers and Unions	Time of Appearance and Union According to							
			Engelbach Shelton	Baetjer Waters	Knox	Rotch	Poland	Cohn	Allen	
6 years (72 mo.)	Wrist (AP)	*Trapezoid.....	6th yr.	6th yr.	6th yr.	6-8 yr.	4 yr. 6 mo.	5-6 yr.	5-6 yr.	
		*Dist. ep. ulna.....	6th yr.	4th yr.	4th yr.	5-7 yr.	4-5 yr.	6-7 yr.	6-8 yr.	
	Elbow (AP)	*Int. cond. humerus....	6th yr.	5th yr.	5th yr.	5th yr.	7-11 yr.	5-8 yr.	
	Shoulder (AP)	*Union head and gr. tub. humerus.....	6th yr.	6th yr.	5th yr.	6th yr.	4-7 yr.		
7 years (84 mo.)	Hip (AP)	*Union ischium and pubis.....	7th yr.	7-9 yr.	7-8 yr.	7-8 yr.	5-7 yr.	7-10 yr.	
8 years	Knee (AP)	*Depression for semi- lunar cart.....	8th yr.	8th yr.		
(96 mo.)	Ankle (Lat)	*Ep. os calcis.....	8th yr.	10th yr.	10th yr.	9th yr.	8-9 yr.	7-10 yr.	
9 years (108 mo.)	Elbow (Lat)	*Trochlea.....	9th yr.	10-11 yr.	11-12 yr.	10th yr.	8-9 yr.		
		*Olecranon.....	9th yr.	8-9 yr.	10th yr.	10th yr.	8-10 yr.	10th yr.	
10 years (120 mo.)	Wrist (AP)	*Pisiform.....	10th yr.	8-11 yr.	12th yr.	12th yr.	13th yr.	10-13 yr.	9-13 yr.	
	Hip (AP)	*Epiphysis lesser tro- chanter femur.....	10th yr.	11-13 yr.	13-14 yr.	12-14 yr.	13th yr.	9-11 yr.	8-14 yr.	
11 years (132 mo.)	Elbow (AP)	*Ext. cond. humerus....	11th yr.	12-14 yr.	13-14 yr.	12-13 yr.	7-11 yr.	12-14 yr.	
12 years (144 mo.)	Knee (Lat)	*Tubercle tibia.....	11th yr.	11th yr.		
		Elbow (AP)	*Union trochlea and capitellum.....	12th yr.	16th yr.	16-17 yr.	11-13 yr.	

Table showing normal osseous development. Age of patients from birth to 20 years. Taken from the article by Shelton, 1931.



Fig. 3. Hypophyseal infantilism. Patient is aged 17 years and 8 months. His height is $54\frac{1}{4}$ inches, and his weight $85\frac{1}{2}$ pounds. Note his childish appearance; also absence of facial and body hair, and retarded genital development. U. C. O. P. D. 209,620.

Clothed figure to the right shows normal development.

metabolism on skeletal growth. Yet it must be admitted that, unless the metabolic disturbance is of such a grave nature as to be entirely obvious, its rôle as a morbid factor in retarded ossification shrinks to relative insignificance. Contrariwise, the hormonal influences on the speed of metabolism are well known. Consequently, it usually becomes necessary to explain either a retarded or advanced bone age as resulting from disturbances in function of one or several of the ductless glands.

In order to avoid confusion in briefly presenting the effect of endocrine disturbances on osseous development, diseases of the ductless glands for this purpose may be rather arbitrarily divided into (a) those which result in delayed ossification, and (b) those which produce premature ossification. A third group of diseases, non-endocrine in nature or whose incretory origin is uncertain, but which seemingly may influence bony development, will also be mentioned.

A. *Endocrine Diseases Resulting in Delayed Ossification (Retarded Bone Age).*—While it is to be admitted that apparently normal children may, on rare occasions, give evidence of a slightly retarded bone age, the most common endocrinopathy which results in a delayed appearance of

TABLE III.—ROENTGENOGRAPHIC STUDIES IN NORMAL OSSEOUS DEVELOPMENT—FEMALE ADOLESCENT (13–18 YEARS)

Birthday	Joint	Union Ep. with Diaphysis	Time of Union According to						
			Shelton	Baetjer Waters	Knox	Rotch	Poland	Cohn	Allen
13th–15th	Elbow (Lat)	Olecranon	13–14 yr.	17th yr.	16th yr.	14th yr.	17th yr.
	Ankle (Lat)	Ep. os calcis	13–14 yr.	18th yr.	15th yr.	15th yr.	15th yr.	15–20 yr.
14th–16th	Elbow (AP)	Ext. condyle	14–15 yr.	18–19 yr.	16–17 yr.	16–17 yr.	16–18 yr.
		Head radius	16–17 yr.	17–18 yr.	14th yr.	15–20 yr.
	Hip (AP)	Trochanters	14–15 yr.	17–18 yr.	17–18 yr.	18th yr.	18–19 yr.	15–16 yr.	17–22 yr.
		Head femur	17–18 yr.	18th yr.	19th yr.	15–16 yr.	18–19 yr.
	Wrist (AP)	Ep. phalanges	14–15 yr.	16–17 yr.	18–20 yr.	18th yr.	18–20 yr.
		Ep. metacarpals	17–18 yr.	18th yr.	18th yr.	14–20 yr.
16th–18th	Ankle (AP)	Ep. phalanges	14–15 yr.	17th yr.	18–20 yr.	16–23 yr.
		Ep. metatarsals	17th yr.	14–21 yr.
	Ankle (AP)	Dist. ep. tibia	16–17 yr.	17–18 yr.	18th yr.	18th yr.	18th yr.
17th–19th		Dist. ep. fibula	18–25 yr.	20th yr.	19–21 yr.	18th yr.	20–22 yr.
	Wrist (AP)	Dist. ep. radius	17–18 yr.	17–18 yr.	20th yr.	19–23 yr.	20–21 yr.	21–25 yr.
		Dist. ep. ulna	18th yr.	20th yr.	18–20 yr.	20–21 yr.	18–24 yr.
	Shoulder (AP)	Head humerus	17–18 yr.	20th yr.	18–20 yr.	19–20 yr.	18–19 yr.
		Gr. tuberosity	20th yr.	20th yr.
	Knee (AP)	Dist. ep. femur	18–20 yr.	20th yr.	20–23 yr.	19th yr.	20–24 yr.
		Prox. ep. tibia	17–18 yr.	18–20 yr.	20th yr.	21–22 yr.	19th yr.	19–24 yr.
		Prox. ep. fibula	18–25 yr.	25th yr.	20–23 yr.	19th yr.	20–22 yr.

Table showing normal osseous development. Age of patients from birth to 20 years. Taken from the article by Shelton, 1931.

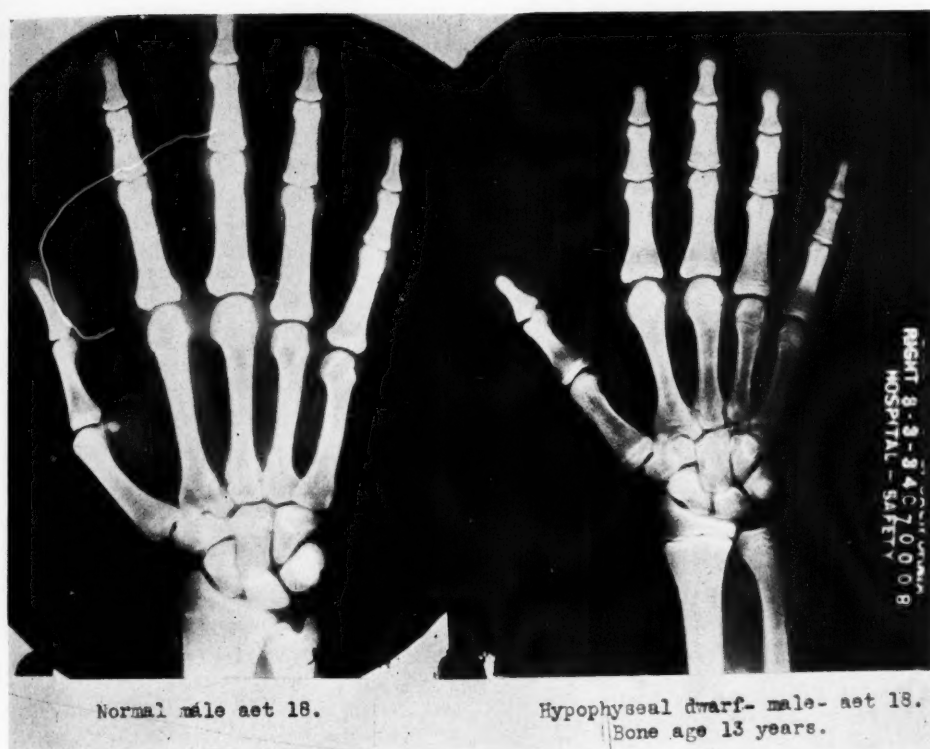


Fig. 4. Hypophyseal infantilism. The bone age studies of the patient shown in Figure 3.

the osseous nuclei is juvenile myxedema. Even the milder forms of hypothyroidism which fail to produce the clinical picture of active myxedema almost uniformly result in a demonstrable delay in epiphyseal closure.

A typical case of juvenile myxedema, for which the term "sporadic cretinism" is frequently synonymously although erroneously used, displays such glaring abnormalities that once seen it should be immediately recognized. The child (Fig 1) is somewhat obese, mentally retarded, and dwarfed in stature (3). The skin is thick and dry, and perspiration is usually absent. The hair is sparse, coarse, and dry. The face is broad and round with a low wrinkled forehead. The eyes are sunken and wide apart, the lid slits are narrow and the lids themselves puffy. The nose has some resemblance to the saddle nose of congenital syphilis and achondroplasia.

The tongue is large, thick, and juicy, and often protrudes so that the mouth gapes open and drools. The combination forms a face which is at once stupid and repulsive.

The condition of the teeth depends upon the age of onset of the disease. Delay in eruption of both the temporary and permanent teeth is almost a constant finding.

The neck is short and thick, the thorax flat. The abdomen is markedly protuberant ("pot belly") and frequently shows an umbilical hernia. The arms and legs are short, the hands puffy, and the spine may show lordosis or kyphosis. The skeleton remains dwarfed.

The genitalia are sometimes retarded in development, and the secondary sex characters and transformations which occur at puberty frequently are markedly delayed. Occasionally there may be observed a slight sexual precocity, especially in girls, with



Fig. 5. Pre-adolescent eunuchoid. Bone age studies of the patient shown in Figure 6.

TABLE IV.—ROENTGENOGRAPHIC STUDIES IN NORMAL OSSEOUS DEVELOPMENT—MALE ADOLESCENT (15–20 YEARS)

Birthday	Joint	Union Ep. with Diaphysis	Time of Union According to						
			Shelton	Baetjer Waters	Knox	Rotch	Poland	Cohn	Allen
14th–16th	Elbow (Lat)	Olecranon.....	14–15 yr.	17th yr.	16th yr.	14th yr.	17th yr.
	Ankle (Lat)	Ep. os calcis.....	14–15 yr.	18th yr.	15th yr.	15th yr.	15th yr.	15–20 yr.
15th–17th	Elbow (AP)	Ext. condyle.....	15–16 yr.	18–19 yr.	16–17 yr.	16–17 yr.	16–18 yr.
		Head radius.....	16–17 yr.	17–18 yr.	14th yr.	15–20 yr.
	Hip (AP)	Trochanters.....	15–16 yr.	17–18 yr.	17–18 yr.	18th yr.	18–19 yr.	15–16 yr.	17–22 yr.
		Head femur.....	17–18 yr.	18th yr.	19th yr.	15–16 yr.	18–19 yr.
	Wrist (AP)	Ep. phalanges.....	15–16 yr.	16–17 yr.	18–20 yr.	18th yr.	18–20 yr.
		Ep. metacarpals.....	17–18 yr.	18th yr.	18th yr.	14–20 yr.
17th–19th	Ankle (AP)	Ep. phalanges.....	15–16 yr.	17th yr.	16–23 yr.
		Ep. metatarsals.....	17th yr.	18–20 yr.	14–21 yr.
	Ankle (AP)	Dist. ep. tibia.....	17–18 yr.	17–18 yr.	18th yr.	18th yr.	18th yr.
		Dist. ep. fibula.....	18–25 yr.	20th yr.	19–21 yr.	18th yr.	20–22 yr.
18th–20th	Wrist (AP)	Dist. ep. radius.....	18–19 yr.	17–18 yr.	20th yr.	19–23 yr.	20–21 yr.	21–25 yr.
		Dist. ep. ulna.....	18th yr.	20th yr.	18–20 yr.	20–21 yr.	18–24 yr.
	Shoulder (AP)	Head humerus.....	18–19 yr.	20th yr.	18–20 yr.	19–20 yr.	18–19 yr.
		Gr. tuberosity.....	20th yr.	20th yr.
	Knee (AP)	Dist. ep. femur.....	18–20 yr.	20th yr.	20–23 yr.	19th yr.	20–24 yr.
		Prox. ep. tibia.....	18–19 yr.	18–20 yr.	20th yr.	21–22 yr.	19th yr.	19–24 yr.
		Prox. ep. fibula.....	18–25 yr.	25th yr.	20–23 yr.	19th yr.	20–22 yr.

Table showing normal osseous development. Age of patients from birth to 20 years. Taken from the article by Shelton, 1931.

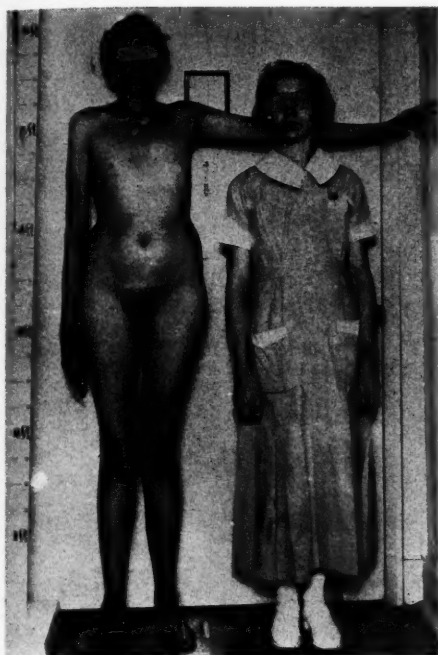


Fig. 6. Pre-adolescent eunuchoid. The patient is 34 years of age and has never menstruated. Note the eunuchoid proportions the long bones and the absent mammary development. Bone age is about 19 years.

The clothed figure to the right shows normal development.

early development of breasts and pubic hair and early onset of irregular but profuse menstruation.

The most striking evidence of skeletal retardation is seen in the delayed appearance of the various ossification centers (Fig. 2). No study of a case of juvenile myxedema is complete without roentgenographic estimation of the bone age, for demonstration of a retarded osseous development is frequently of fundamental importance. Determination of the basal metabolic rate in infants is not generally possible because of the circumstantiality of the test. Furthermore, as recently emphasized by Canelo and Lissner (4), the mental retardation so frequently pronounced mitigates against proper co-operation by the child and often prevents performance of the test altogether.

Not infrequently many of the signs of

juvenile myxedema may be absent; in fact, myxedema should be considered a symptom, not a disease. Infantile or juvenile



Fig. 7-A. Adrenal cortical hyperplasia in a female aged five years. The patient's height is $49\frac{3}{8}$ inches and her weight is $55\frac{1}{2}$ pounds. Well developed pubic hair.

hypothyroidism may vary in severity within wide ranges, so that the myxedematous condition should not be considered the essential feature in the diagnosis of thyroid insufficiency. But uniformly there is to be found a definite retardation of ossification which, generally speaking, parallels the degree of thyroid deficiency.

The dwarfism of hypothyroidism is to be differentiated from that resulting from



Fig. 7-B. (Same case as shown in Figure 7-A.) Clitoris is markedly hypertrophied. U.C. O.P.D. 153,553.

pre-adolescent hypopituitarism, hypophyseal infantilism (Fig. 3). In the latter condition there may be a marked inhibition of skeletal growth, but this childhood form of dwarfism is accompanied by a slender figure without puffiness, and is invariably characterized by arrested sexual development. This infantilism, which results from deficiency of the growth and sex hormones of the adenohypophysis, occurs far more frequently than is generally supposed.

The skeleton of the hypophyseal dwarf is invariably delicate and gracile. The chin may be markedly recessive, the palatal arch narrow and highly vaulted. The teeth are apt to be overcrowded and forced out of alignment by reason of the inadequate development of the jaws. The skin is curiously smooth and delicate, and bruises easily. The saddle nose, thick tongue, and myxedematous puffiness are absent.

The mentality of such children is ordinarily normal. Many are above the average mentally; only rarely does slight retardation occur, and the demeanor of this type of dwarf is composed, bright, and cheerful, as is to be expected since the psychic and mental development remains normal.

The genital aplasia is extremely con-

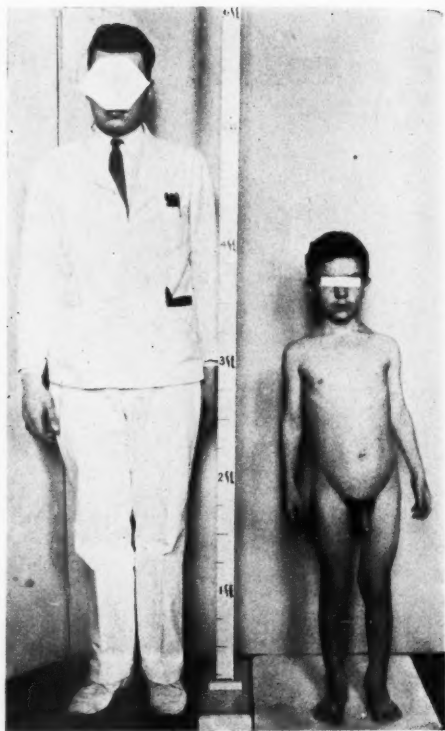


Fig. 8. Adrenal cortical adenoma in a male, aged four years and 11 months. The patient's height is $47\frac{1}{8}$ inches and his weight is 59 pounds. He has a well developed mustache and pubic hair; also adult genitalia. The skull plates are normal. Left adrenal tumor demonstrated by retrograde pyelogram. Bone age is between 11 and 12 years (See Fig. 10). (Through the courtesy of Dr. H. Lissner, San Francisco, California.)

spicuous; the external and internal genitalia remain persistently retarded. The secondary sex characters may never develop. In fact, these patients persist, even into adult life, in a childish state of skeletal and sexual development, unless prolonged and intensive administration of pituitary growth-stimulating and gonadotrophic hormone is employed.

Roentgenographic studies of the skull may be entirely negative. The sella turcica may appear small, with bridging of the clinoid processes. Yet, it should be emphasized that the size of the bony encasement is no direct clue to hormonal function. Epiphyseal closure is apt to proceed at a fairly normal rate but a slight

retardation is not uncommon. However, this retardation in bone age (Fig. 4) is usually much less than that in the hypothyroid dwarf.

tinue for many years after it should have ceased.

The pre-adolescent eunuchoid (Fig. 6) is tall, slender, and undernourished, with



Fig. 9-A.

Fig. 9-A. Normal female, aged 5 years.



Fig. 9-B.

Fig. 9-B. Advanced bone age caused by adrenal cortical hyperplasia. Roentgenographic studies of patient shown in Figure 7. Chronological age is 5 years; bone age is from 13 to 14 years.

Another rather frequent cause of delayed ossification is the preadolescent failure of the hormonal activity of the gonads. This, however, results not in dwarfism but in undue tallness with disproportionately long extremities. Closure of the epiphyses is greatly delayed even to late adult life (Fig. 5), probably as a result of loss of the growth-checking principle which supposedly emanates from the interstitial tissue of the ovaries and testes. In fact, roentgenograms may demonstrate ununited epiphyseal junctures as late as 25 or 30 years of age, and in the presence of an active growth-stimulating principle from the anterior hypophysis this delay in epiphyseal closure permits growth to con-

a narrow flat chest, long slender fingers, and long narrow feet. The complexion is apt to be pasty and acned; the vitality is meager. The genitalia remain infantile; the secondary sex characters remain immature. In girls, the menarche occurs very late if at all. The tall stature and long extremities readily differentiate them from both the hypothyroid and the hypopituitary dwarfs, even though delayed epiphyseal closure is common to all three. Interestingly enough, the bone nuclei are usually normal for the age in pre-adolescent hypogonadism, a condition which is strikingly different from the delayed appearance of the nuclei associated with infantile or juvenile hypothyroidism.



Fig. 10. Accelerated osseous development resulting from adrenal cortical hyperactivity. Roentgenographic studies of patient shown in Figure 8. Chronological age is 4 years and 11 months; bone age is between the ages of 11 and 12.

B. Endocrine Conditions which Produce Premature Ossification (Advanced Bone Age).—Abnormal function in childhood of at least three ductless glands is capable of producing a startlingly premature epiphyseal closure. They are the pineal gland, the cortical portion of the adrenal glands, and the gonads. Tumor or hyperplasia with the consequent increase in incretory function of each of these glands produces a precocious "skeletal ripening which for a time simulates gigantism." It ends, however, as prematurely as it began, giving the effect of a transient gigantism, the final stature being in fact rather small since the skeletal growth is not permitted to continue over as long a period as usual.

Radiologic demonstration of the sometimes markedly accelerated bone age common to pinealism, suprarenal hyperactivity, and hypergenitalism helps not at all in differentiating these three conditions one from the other. All are characterized by precocious puberty (Fig. 7), and by early sexual maturity both as regards the size of genitalia and development of secondary sex characters, with mental and psychic states being correspondingly advanced. Determination of the causation of this premature development of the entire organism depends upon the demonstration of localizing signs, such as increased intracranial pressure and quadrageminal

signs in involvement of the pineal, the presence of an abdominal tumor in the case of suprarenal or ovarian neoplasm, or the finding of a tumor of the testicle. The final diagnosis may be entirely dependent upon the results of roentgen examination of the skull and especially retrograde pyelograms.

Tumors of the suprarenal cortex developing in childhood occur far more frequently in girls. However, Lissner (5), after a meticulous search of the literature, found eight unquestionable instances of adrenal cortical tumors causing sexual precocity in boys. He reports a ninth case, the only recorded one in which the tumor was successfully removed (5-a).

On the other hand, pineal tumors have consistently occurred in boys. This is a rare disease of childhood, which, in the cases reported, has been characterized clinically by general symptoms due to increased intracranial pressure, focal symptoms due to pressure on neighboring structures, as well as the endocrine manifestations of macrogenitosomia præcox.

Most of the gonadal tumors have occurred in girls; in fact, most of the cases of precocious puberty in girls have been found to result from ovarian growths, probably granulosa-cell tumors. Hyperfunction of the internal genitalia with consequent abnormally early menarche is usually associated with this type of tumor. Premature onset of the menstrual cycle points to pathologic involvement of the ovaries, whereas suprarenal cortical tumors are more apt to produce hypertrophy of the external genitalia. In addition, the latter (suprarenal cortical tumors) seem to produce a "tendency to the development of the male at the expense of the female characters in the girls (virilismus) and an intensification of the male characters in the boy (pubertas præcox virilis)." Girls are masculinized, as is exemplified by the growth of beard and mustache, hair on the chest, abdomen, and upper thighs, and by hypertrophy of the clitoris, deepening of the voice, and a masculine body configuration. Boys of four or five (Fig. 8)

may have the external genitalia of the adult, with abundant hair on the mons pubis, in the axilla, and on the upper lip

tion may be a factor. The obesity and overgrowth in height may precede the premature appearance of menses often by



Fig. 11-A.

Fig. 11-A. Normal female, aged 12 years.



Fig. 11-B.

Fig. 11-B. Accelerated osseous development, resulting from granulosa cell tumor. Menarche at 5 months. The patient had pubic hair and some mammary development at 2 years. Chronological age is 11 years and 11 months. The patient's height and weight are normal but the trunk is disproportionately long. External genitalia are normal. Bone age is 17 years.

and the chin. The accelerated development found in tumors of each of the three glands, pineal, adrenal cortex (Fig. 10), and gonad (Fig. 11), is accompanied by advanced ossification, dentition, and bone growth, all of which may be adequately demonstrated by proper roentgen examination (6).

Recently, Reilly (7) has called attention to a peculiar and as yet unexplained clinical syndrome, having as its cardinal features advanced ossification accompanied by increased height, occurring only in girls and associated with an early menarche, premature development of secondary sex characteristics, obesity, and definitely reduced metabolic rate. The latter is not accompanied by the usual signs of hypothyroidism (Figs. 12 and 13).

A similar syndrome occurring in boys has not been discovered, consequently, it is possible that a disturbed ovarian func-

tion may be a factor. The obesity and overgrowth in height may precede the premature appearance of menses often by many years, so that a primary anterior lobe hyperpituitarism, involving both growth-stimulating and maturity-provoking hormones, might theoretically account for the rapid growth, advanced ossification, and somewhat early sexual maturity. It is difficult, however, to explain the obesity and lowered basal metabolic rate on this basis. In as much as pathologic material is not available to assist in the determination of the possible etiologic factors, the syndrome for the moment must remain an enigma.

Comparable after a fashion to the syndrome of advanced ossification, precocious skeletal development and early maturity, described by Reilly, is the condition thoroughly studied by Le Marquaud (8). This remarkable child of two and one-half years of age had a bone age estimated at 10 years. His genitalia were developed to proportions considered as about one-half

the adult size, and his psyche, in certain respects at least, was greatly advanced. Obesity was a minor factor, for while the

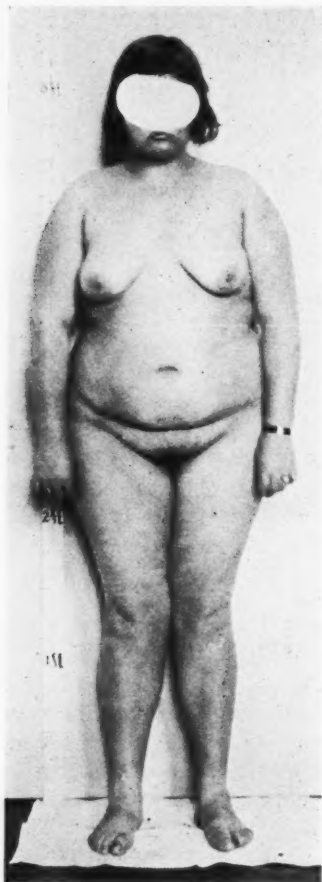


Fig. 12. "Reilly Syndrome." The patient is aged 13 and one-half years. Her height is 63 inches and her weight is 204 pounds. Menarche at 11 years and 9 months. Her B.M.R. is 32 per cent minus. Bone age is 18 years plus (See Fig. 13). Her IQ is 123.

child was large, his unusually great muscular development adequately accounted for his increased size. Death finally supervened in the child's fifth year (4 years, 10 months). Necropsy did not reveal the expected finding of an adrenal cortical tumor or a pinealoma, but a neoplasm "occupying the interpeduncular

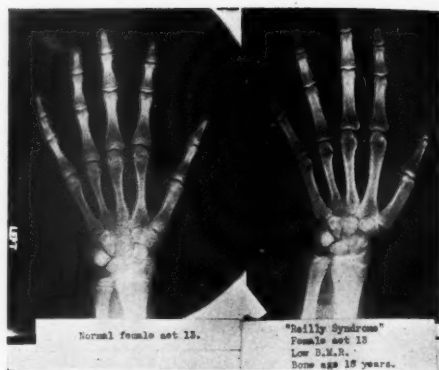


Fig. 13. "Reilly Syndrome." Bone age studies of patient shown in Figure 12.

space attached to the right corpus mamillare and to the tuber cinereum." This unusual pathologic development completely forestalls any attempt at explanation of the hormonal factors etiologically evident in the production of a syndrome, which so closely resembled that produced by tumors of the pineal gland, the cortical portion of the adrenal glands, or of the gonads.

One or two other diseases, frequently, though for the present erroneously, thought to result from disturbances in endocrine function, may be accompanied by alterations in bone development. Thus, in rachitic dwarfism, in which the intelligence and sexual development remain normal, there may be no constant changes in the time appearance of the bone nuclei or the union of the epiphyses. Yet both may be slightly premature or slightly retarded according to the degree of proliferation of abnormal cartilage and the intensity of the reparatory process. Joachimstal describes the roentgen picture as showing a "washing out of the boundaries between the bone nuclei and cartilages and broad light zones at the site of epiphyses, apparently representing excessively proliferated cartilage."

In the achondroplastic dwarf, the ossification of the epiphyses proceeds very irregularly, some unions occurring prematurely, and others abnormally late. The cause of this condition is not known but the diagnosis offers little difficulty. It is apt

to be familial or hereditary; intelligence develops normally, as does genital development and function. The dwarfism results



Fig. 14. Renal dwarfism. Patient is aged 11 years. His height is 48 inches, and his weight is 58 pounds. There was marked albuminuria. Phthalein was 4 per cent in two hours. His blood N.P.N. was 208 mg. per cent. Hemoglobin was 25 per cent Sahli; R.B.C. 1,800,000. B.M.R. was 21 per cent minus (Benedict Talbot Standards). Bone age is 7 years.

from the extraordinary inhibition in the growth of the extremities due to a "growth disturbance of the cartilages at the ossification boundary, especially those of the long bones, setting in in the earliest fetal life" (Falta).

The pathogenesis of mongolian idiocy

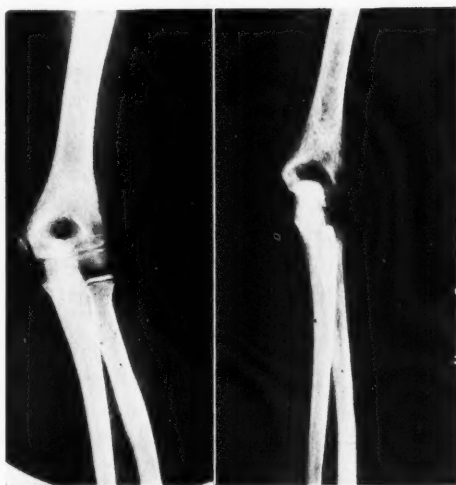


Fig. 15. Retarded osseous development in the case of renal dwarfism shown in Figure 14.

is likewise obscure. In this disease, the mentality is impaired sometimes to the point of idiocy; skeletal growth may be retarded, and there is a mongolian slant to the eyes which, when present in a Caucasian, is diagnostic. There may be a slight delay or at times even a slight prematurity in appearance of the bone nuclei. Usually there is no delay in epiphyseal closure. The most remarkable feature of the skeleton of the mongolian idiot is the hand. "The metacarpus is small; the metacarpal fingers are short and thick but taper toward the extremities. The thumb and little finger are very short; the little finger is incurved toward its neighbor, its tip seldom reaching to the middle of the second phalanx." (Telford-Smith finger: these peculiarities are nicely revealed by roentgenograms.)

True mongolism as well as birth injuries and other forms of mental deficiency do not consistently retard the unfolding of the osseous system, although hypothyroidism is occasionally associated with such conditions and must consequently give a confused picture. Rickets may be easily excluded by clinical and roentgenologic observations peculiar to the disease.

Renal dwarfism may be associated with osseous retardation. In fact, a child suf-

fering with this condition, also known as renal rickets may, at first glance, readily be mistaken for an example of hypophyseal infantilism (Fig. 14). Such a dwarf was recently studied. His bone age (Fig. 15) was four years behind his chronological age which was eleven years. However, the low phthalein output (3 per cent in 2 hours), the albuminuria and high protein retention, together with the marked secondary anemia, afforded ample evidence of the true diagnosis.

Other types of dwarfism should be mentioned, although bone-age studies offer little help in adequately differentiating them. Thus, in true infantilism, which Falta describes as a standing still at the infantile stage of development, the patient retains childish skeletal dimensions, childish genitalia and childish psyche, and the osseous development is retarded. The endocrine system participates in but does not originate this condition. On the other hand, in primordial dwarfism, a congenital condition in which the infant is dwarfed at birth, the individual matures sexually and intellectually but remains skeletally dwarfed. As is to be expected, the appearance of bone nuclei and closure of epiphyses proceed normally.

Paultauf's dwarfism presents an unsolved problem. These children are normal at birth; in youth, growth suddenly ceases for a varying period of time only to be resumed later. Genitalia and secondary sex characters are retarded. The appearance of the bone nuclei is delayed and the epiphyses may remain open into adult life. The moribific factor in this type of dwarfism is unknown.

Finally, that peculiar form of dwarfism described by Morquio (9), in 1929, is occasionally encountered. This is a very rare disease which has been adequately studied by Ruggles (10). All the cases reported have a characteristic and similar appearance, looking like members of the same family. Skeletal and sexual development is markedly retarded; the intelligence is usually unimpaired, and there is a loss of power in the arms and legs without

atrophy. The hair is fine but the skin is dry and coarse, although the basal metabolic rate has varied from 10 to 20 per cent plus. The roentgen findings are as characteristic as the outward appearance; the bone age is very markedly retarded. The condition is due to a profound disturbance of epiphyseal development, the etiology of which is at present entirely unknown.

This rather brief summary of the more important endocrinopathies in which osseous development is abnormal indicates that the value of roentgen-ray studies in the differential diagnosis of endocrine disturbances is always of paramount importance. And at times the radiographic examination may be an absolute necessity before a complete and adequate survey of the true condition becomes apparent. This is especially true in infants in whom more complicated procedures are impossible. Furthermore, repeated roentgenographic studies at intervals of six months to one year of children who give evidence of retarded or accelerated osseous, mental and sexual development, affords an excellent criterion of the effectiveness of the indicated therapy.

The roentgen ray has been proven to be of inestimable value both diagnostically and therapeutically. To the endocrinologist, however, the radiologic comparison of the endocrinopathic and normal subject, wherein is demonstrated a delayed or precocious bony development, probably offers more aid than any other use to which the x-ray can be put. The importance of roentgenographic bone-age studies cannot be overemphasized.

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RADIATION CASTRATION IN THE TREATMENT OF MALIGNANCY OF THE BREAST¹

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THE changes in the last few years in the treatment of carcinoma of the breast by surgery alone, radiation alone, or by an intelligent combination of the two methods indicate that neither the surgeons nor the radiologists are particularly well satisfied with the results obtained. No doubt part of our failure is to be found in the fact that the radical operation is too often not complete, but this also seems to be just as true of radiation. When the

of these cases were considered by the surgeons to be in an early enough stage for treatment by the radical operation alone; 11 were considered to be borderline cases, which were operated upon and received post-operative radiation, and eight cases became operable after a full course of radiation. In other words, less than 50 per cent of the cases of carcinoma of the breast seen in this important surgical clinic in 1931 received some form of surgery, and



Fig. 1. Roentgenogram taken on Sept. 21, 1931, showing a large area of destruction above the right acetabulum. Before castration.

operation is most meticulously carried out, and when radiation is just as meticulously given according to the methods best accepted to-day, we can honestly look forward to a higher percentage of cures, far in advance of the present average figures. In a recent article, Professor Hans R. Schinz points out that, in his surgical clinic in Zürich, 50 cases of carcinoma of the breast were seen in 1931. Only two

a high percentage of these became surgical only after radiation. Undoubtedly there will be a large number of cases in this group which sooner or later will be candidates for palliation therapy of some kind, and undoubtedly the experience of this clinic is not radically different from any other similar clinic abroad or in this country.

A summation of all these cases in this country alone would leave a tremendous number of unfortunate patients for whom any form of palliation, other than a muti-

¹ Presented before the Radiological Society of North America, at the Twenty-first Annual Meeting, at Detroit, Dec. 2-6, 1935.



Fig. 2.

Fig. 2. Roentgenogram taken on Oct. 2, 1931, showing large area of destruction just below the lesser trochanter of the right femur. Before castration.

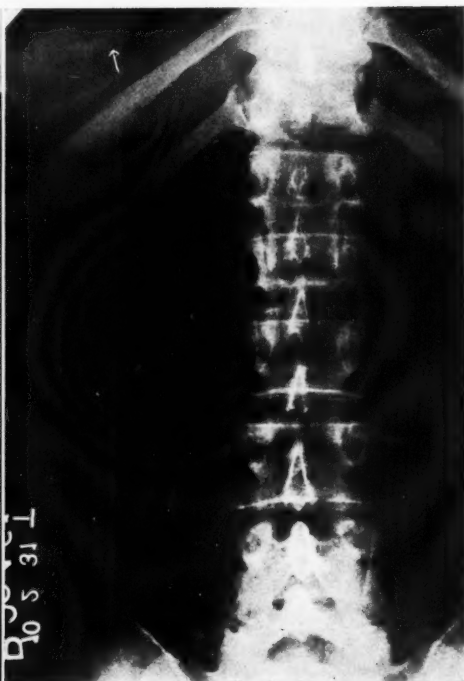


Fig. 3.

Fig. 3. Roentgenogram taken on Oct. 2, 1931, showing destruction in the right tenth rib and second lumbar centrum. Before castration.

lating procedure or heavy drug therapy, would be most welcome—and to their attending physicians as well. We as radiologists are fortunate enough to have at our disposal such a method for patients who have not reached the menopause. Roentgen-ray castration represents such a method.

It is well known that a definite relation exists between the activity of the ovaries and the histology and physiology of the breast; that the parenchyma of the breast may undergo rapid growth and transformation under certain physiologic conditions of ovarian activity, and that there is strong support for the theory that ovarian hormonal influences may play a large part in producing hypertrophy, hyperplasia, and neoplasms in the breast. These are axiomatic to-day and need no further discussion. Long before the introduction of the roentgen method, Schinzinger, at the

Surgical Congress in Germany, in 1889, proposed bilateral oophorectomy as an accessory method in the treatment of cancer of the breast in younger women, because he noticed that the disease progressed more rapidly and was more frequently fatal in younger women, and he thought that by oophorectomy the patient would grow old more rapidly.

The same suggestion was made independently in England, in 1896, by Beatson, who also believed that the thyroid produced a hormone, the action of which on the mammary gland was contrary to that of the ovaries, and this author, therefore, prescribed thyroid medication with the hope of augmenting the effect of castration. It was Beatson's belief that carcinoma of the breast was due wholly or in part to an abnormal function of the ovaries, and, after considerable experience, concluded that the method was justified



Fig. 4.

Fig. 4. Roentgenogram taken on April 13, 1932, showing complete regeneration just above the right acetabulum and in the right femur. After castration.

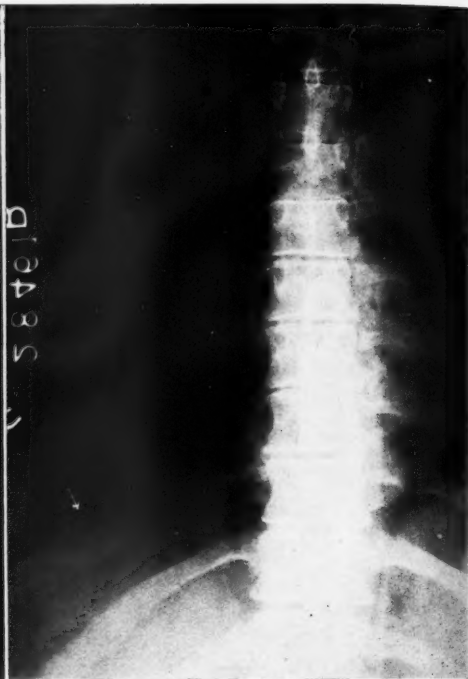


Fig. 5.

Fig. 5. Roentgenogram taken on April 13, 1932, showing regeneration in tenth right rib. After castration.

only in menstruating women over forty years of age. Further figures were given shortly afterwards by other English surgeons who followed Beatson's teaching. Boyd reported a series of 54 cases, with definite improvement in 35 per cent; Thomson reported 80 cases, with 24 per cent improvement, and Lett, 99 cases, with 23 per cent improvement. Other authors reported similar series, among them being Michels, Herman, Reynés, Smith, Annandale and Donald, and many others.

The earliest report of roentgen-ray castration is by Foveau de Courmelles, in 1904. Meyer was the first in Germany, and additional work has been done and reported by many authors: Wintz, Lapeyere, Frangenheim and Kaplan and others, some of which will be mentioned later. Roentgen-ray sterilization has replaced the surgical method, probably for the main

reason that bilateral oophorectomy is associated with about a 6 per cent mortality (Lett), whereas there is no risk with radiation, and even though there is grave doubt in the minds of some as to the effects of the two methods being the same, there is as yet no adequate proof that the radiation method is not as effective as the surgical one.

In reviewing the literature one is impressed by the fact that roentgen castration is used in two ways: (1) as an immediate measure in therapy before the appearance of metastases, and (2) as a palliative measure after the appearance of widespread metastases.

IMMEDIATE CASTRATION

Judging from the early reports of bilateral oophorectomy, there seems to be no doubt that the primary tumor regresses in some cases rather rapidly. This same

effect has been noted by many authors since the radiation method has been used. Nearly all agree that when ovarian radiation is used along with radiation to the primary lesion, the latter seems to react more readily and the patient shows an earlier return to a general state of good health.

These facts have been particularly well brought out by Ahlbom, who states, however, that there is no definite evidence that the patient's life is prolonged. On the other hand, life will undoubtedly be prolonged in those cases in which sterilization prevents future pregnancies. It is a matter of common experience that a carcinoma of the breast in a pregnant woman is a most serious combination. Trout reports 15 cases of breast cancer with subsequent pregnancies. Of these, 13 developed the lesion in the opposite breast and 12 died in a very short time. There seems to be little doubt, therefore, that previous experience with either bilateral oophorectomy or radiation castration warrants the assumption that the primary lesion is apt to regress more rapidly and that fulminating recurrence with pregnancy can be avoided.

AS A PALLIATIVE MEASURE

It is with this procedure that the author has had most experience, because in spite of the fact that the patient can be assured that there is little chance she will have menopausal symptoms, it has been my experience that a large majority will not accept early castration, either because of some firm religious conviction or because they desire to have one or more children no matter what the penalty may be. The position of radiation therapy is stronger than ever to-day, and if we are to believe the signs in the recent literature there are many reasons to believe that radiation will eventually dominate the field of cancer anywhere in the body, the same as many believe it does at present in cancer of the cervix and the body of the uterus. The late Joseph Colt Bloodgood made the statement that he believed the time for removing a breast



Fig. 6. Roentgenogram taken on Aug. 29, 1933, showing extensive metastatic malignancy in the lumbar spine.

for even a microscopic malignancy was almost over. No radical surgical procedure should be considered, no matter what the size or duration of the primary lesion, until roentgen examination has ruled out the existence of metastatic disease in the usual sites. If metastases are present, then roentgen castration has a great deal to offer. Obviously it is not practical to radiate all areas in a case of extensive bony metastases, nor is it wise to attempt to radiate local areas in similar cases until castration has been tried. Unfortunately the disappearance of clinical symptoms after castration is not always consistent, but when relief is obtained the result is often so striking that the method should always be used. Remarkable cases have been reported by many authors—Deland, Martin, and others. The number in the author's series has not been large, but one is so striking that it bears reporting.

Mrs. A. F., white, aged 44 years, a washerwoman, operated on about two

years previous, was seen in September, 1931, with all the typical clinical signs of advanced malignancy, and with extensive

appearance of pain, associated with (2) a return to general good health, (3) recalcification of bony destruction, and (4) no



Fig. 7. Roentgenogram taken on Aug. 29, 1935, showing extensive metastatic malignancy in the pelvis.

evidence of widespread bony metastases of the osteolytic type. She was suffering from excruciating hip pain—was admitted from the dispensary with such intense pain that not even heavy doses of morphine could alleviate it. She was given a castration dose according to the accepted method, namely, 900 r units front and back, divided into six sittings of 300 r units each, alternating the fields front and back with 1 mm. Al and 0.5 mm. Cu as filter, 200 kv. p., 20 ma., and 50 cm. distance. The patient was not seen for nearly two years, after which time she returned for further radiation, stating that her pain was returning and that she was beginning to vomit. In the meantime she had been free of pain and had returned to her work as a washerwoman. Local radiation was tried to the lumbar spine, but she grew rapidly worse and died in an unusually short time, the vomiting having become intractable. The case illustrates nearly all the points noted in other reported cases, which briefly are: (1) dis-

relief from further or local irradiation, followed by (5) rapid death after recurrence of symptoms. Not all patients will show such a remarkable result, but it is seldom that one fails to get some sort of relief. It is important to realize that relief is not dependent upon or necessarily associated with recalcification.

CONCLUSIONS

(1) Many cases of carcinoma of the breast in young women still in the menstrual age show definite improvement after roentgen castration.

(2) This improvement is shown in one of several ways: reduction in the size of the primary lesion, osteoclastic changes in areas previously involved with an osteolytic process, alleviation or disappearance of pain, and a return to general good health.

(3) After a varying length of time the symptoms return and the downhill course is then usually very rapid, thus eliminating the prolonged period of being bedridden.

(4) If carried out early, future pregnancies are avoided.

(5) There seems to be no doubt that an ovarian hormone plays a definite part in malignancies of the breast, and therefore, all women under the age of fifty with carcinoma of the breast should be sterilized.

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HIGH *versus* LOW INTENSITY IRRADIATION IN THE TREATMENT OF CARCINOMA

AN EXPERIMENTAL STUDY ON NON-NEOPLASTIC EPITHELIUM AND MESOBLASTIC TISSUE¹

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WITH the widespread interest in the technic of irradiation therapy developed by Coutard, one of the cardinal principles of which is irradiation at low intensities, it becomes necessary to again review the question of low *versus* high intensity irradiation in the treatment of cancer.

A number of laboratory studies are reported in the literature on the relationship between biologic effects and the intensity of the source of irradiation producing them. In the great majority of instances the biologic indicators employed were plant seedlings, tissue cultures, and lower animal forms, especially *Ascaris* and *Drosophila* eggs. The natural variations in radiosensitivity, occurring during prolonged periods in the latter two indicators, were not appreciated. In addition, much of the work was done at a time when accurate methods of dose determinations were not available. Furthermore, in most instances no special efforts were made to observe possible differences in effects produced by irradiation delivered at low intensity for intermittent periods and effects produced when such doses were administered *continuously* at identical low intensities. For a critical review of the literature up to 1932, the reader is referred to the publication by Pack and Quimby (1). The great bulk of evidence presented would indicate that greater effects are produced by given doses if these are administered at high rather than at low intensities.

Since observations on the relationship between biologic effects and intensity of irradiation made upon tissue cultures and

lower animal and plant forms may not necessarily hold for tissues *in situ* in the intact higher organisms, it becomes apparent that, to bring the study into closer relationship to clinical roentgen therapy, further observations are indicated, made under conditions that more closely approximate those obtained in patients who exhibit carcinoma.

With this purpose in view the experiments recorded below were performed.

EXPERIMENTAL

In the following study, the object of which was to observe the relationship between biologic effects and variation in intensity of irradiation producing them, in tissues of higher organisms *in vivo*, two varieties of biologic indicators were employed: the germinal epithelium of the rat testis, and the erythema reaction in human skin. The former constitutes a very radio-sensitive epithelium distributed in a relatively radioresistant stroma. Cytolethal effects in the germinal epithelium may result with doses insufficient to produce visible reactions in the overlying skin and surrounding stroma. While these effects are the net result of irradiation of the whole organ (testicle), the fact that the visible manifestations are confined to the epithelial elements suggests that this reaction is essentially an epithelial one to irradiation. It might thus exemplify the reactions of radiosensitive malignant epithelial cells distributed in mature non-neoplastic stroma. The analogy between testis and malignant epithelioma has been repeatedly pointed out; in both instances there is a relatively radio-sensitive epithelium distributed in mature connective tissue stroma. The spermatogenic and malignant epithelial cells

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both exhibit a high rate of mitoses; both types of cells are undifferentiated and in each of these tissues there is considerable individual cellular variation in radiosensitivity.

Experiment A.—White rats of various ages as indicated below were employed. They were secured back-downward upon a wooden board. The conditions of irradiation

were: 200 kv., 1.5 mm. Cu, and 1.5 mm. Al. The milliamperage and distance were adjusted to obtain the desired intensity. The *r* unit measurements were made in some instances with an integrating Westinghouse dosimeter, and in other instances with a Wulf ionization chamber. The former was present in the field for the duration of the exposures. When the Wulf instru-

TABLE I

Age	High Intensity	Low Intensity	Ratio	Time after Irradiation	Microscopic Examination
Young adults	B, 101 B, 102 300 r in B, 106 3 min. 47 sec.	B, 103 B, 104 300 r in B, 105 61 min. 30 sec.	1:16	14 days	No gross abnormal changes in sections from either group except for scattered degenerating cells in tubules. In B, 106, many tubules are filled by multinucleated degenerating cells that have desquamated into the lumina.
From 5 to 6 weeks	B, 170 B, 171 300 r in B, 172 3 min. 15 sec. B, 173 B, 179 B, 180 B, 181 300 r in B, 182 3 min. 31 sec. B, 218	B, 174 B, 175 300 r in B, 176 54 min. B, 178 B, 183 B, 184 B, 185 300 r in B, 186 61 min. B, 187 B, 219	1:17	14 days	No difference in changes between sections of the two groups. Occasional tubules contain only Sertoli cells and spermatozoa. There are scattered degenerating cells in the lumina.
Adults from 12 to 18 months	B, 111 B, 112 300 r in B, 113 3 min. 24 sec.	B, 124 B, 130 300 r in 59 min. 30 sec.	1:17.5	17 days	Occasional empty tubules and occasional normal tubule with degenerating cells in lumen. There is no difference in sections of each group.
One month	B, 199 B, 200 B, 201 300 r in B, 202 3 min. 30 sec. B, 203	B, 194 B, 195 B, 196 300 r in B, 197 60 min. 15 sec. B, 198	1:17	14 days	Scattered degenerating tubules. There is no difference between sections from each group.
Adult over 12 months	B, 74 300 r in B, 75 2 min. 55 sec.	B, 79 300 r in B, 80 59 min.	1:20	28 days	Extensive changes of equal magnitude in sections of each group. The majority of the tubules contain only spermatozoa and Sertoli cells, the intermediate types having been destroyed.
Adult over 12 months	B, 139 B, 140 600 r in B, 141 6 min. 10 sec. B, 87 B, 57 600 r in B, 58 5 min. 37 sec.	B, 137 B, 138 600 r in B, 148 59 min. B, 67 B, 55 600 r in B, 56 61 min.	1:9.5	14 days	No difference in magnitude of changes between the groups. A few scattered empty tubules and a few normal tubules with degenerating cells are seen.
Adult over 12 months	B, 49 B, 50 600 r in B, 62 7 min. 35 sec. B, 151 B, 152 600 r in B, 152A 6 min. 30 sec.	B, 92 B, 93 600 r in B, 94 61 min. B, 153 600 r in B, 154 58 min. 30 sec.	1:8	28 days	Extensive changes in all sections and of equal magnitude in both groups. The majority of tubules are completely depopulated of cells, with the exception of a few Sertoli cells in the lining or exhibit Sertoli cells and spermatozoa only.

ment was used, several check readings were made during the irradiation. All readings are surface ones, made upon the wooden

at low intensities an individual of comparable radiosensitivity was not included.

Experiment B.—Five patients each pre-



Fig. 1. Photograph of Case A. R. (129,594), see Table II, showing more intense erythema reaction in irradiated field on left thigh (636 r in 6 min. 50 sec.) than in right thigh, where the reaction is hardly discernible (636 r in 124 min.).

board with the chamber approximately the same distance above it as the rat testes. When one type of dosimeter was employed for a group of animals radiated at high intensities, the same instrument was employed in the corresponding group irradiated at low intensities. At stated intervals the animals were killed, and the testes removed and fixed in acetic acid Zenker's solution, and embedded in paraffin; the sections cut were stained by hematoxylin and eosin.

In these experiments, involving a comparison of 34 pairs of rat testes irradiated at a high intensity, with 33 pairs irradiated under comparable conditions at low intensities (ratio 1:8 to 1:17), no demonstrable differences in the magnitude of biologic effects upon the seminal epithelium were noted. There was a single exception, B, 106, that was irradiated at a high intensity and showed greater effects than those irradiated at a lower intensity in the same group. This single instance can hardly be regarded as of significance since in the other 32 animals a similar result was not obtained. It is felt that in this animal the germinal epithelium was of unusually great radiosensitivity, and that in the group irradiated

sending some form of advanced carcinoma were irradiated over the anterior aspects of the thighs, as indicated in Table II. The conditions of irradiation were: 200 kv., 1.25 mm. Cu + 1.5 mm. Al filter, fields 10×10 cm., milliamperage and focal skin distances being adjusted to obtain the desired intensity. The latter was determined in some instances by a Westinghouse integrating dosimeter, and in other instances by a Wulf instrument, the same instruments used in the animal experiments. When the Wulf ionization chamber was employed, it remained in the field throughout the exposure, readings being taken at intervals to check the intensity.

In this second group of observations (Table II), the biologic indicator employed to observe the effects of variation in intensity was, as stated, the erythema reaction in the human skin. This reaction like the other is probably the net result of effects upon the overlying cutaneous epithelium as well as upon the subcutaneous mesoblastic tissue directly, but, since the gross changes are manifested as a localized vascular congestion and interstitial edema, the erythema reaction might be considered essentially a mesoblastic response. It might

thus exemplify the response of the stroma of a malignant epithelial neoplasm to variations in intensity of irradiation. There are additional reasons why the human skin erythema in itself may be regarded as essentially a mesoblastic reaction, and, therefore, indicative of the reaction of vasculo-connective tissue in general. For example, (1) the erythema reaction precedes visible changes in the cutaneous epithelium; (2) epilation may be induced without erythema, and (3) it is possible to produce pigmentation, exfoliation, and even epithelitis without producing an initial marked erythema.

In this second series of observations, the difference in erythema reaction to varying intensities of the order of 1:18 is definite in all instances and quite marked in two cases; the higher intensities produced the greater reactions. These observations are corollaries to previously reported observations recently summarized by Holthusen and expressed as follows: In the production of equal degrees of skin erythemas by irradiations of unequal intensity, a greater total dose is necessary in the case of low intensity irradiation than in the case of high intensity irradiation.

DISCUSSION

The observations recorded above indicate that when employing as biologic indicators two varieties of tissue *in situ* in the intact organism, namely, germinal epithelium in the rat testicle and the subcutaneous vasculo-connective tissue in human skin, a variation in intensity of a given quantity of x-radiation of the order of 1:8 to 1:17 produces no variation in biologic effects in

the former, whereas a variation in intensity of 1:18 produced constant and in some instances a marked difference in reaction in the latter.

These results indicate the difficulty of making generalizations in regard to biologic effects unless a variety of indicators is employed.

The experiments of Regaud (3) and of Juul (4) upon rabbit testes and transplantable mouse carcinoma, respectively, showed that with high intensities severe skin lesions were produced, whereas with low intensities (and fractionation) the skin was relatively less affected than the testes and tumor. This demonstration of the so-called elective effect of irradiation on sensitive tissues is a comparison of different epithelia, and is a question apart from that considered in this study in which the reactions of sensitive epithelial cells and vasculo-connective tissue are compared. (This difference has not been emphasized in most previous publications.)

Coutard (5) has repeatedly emphasized that one of the major principles in the treatment of carcinoma by fractionated large doses of irradiation is to deliver the required energy in such a manner as to produce minimum disturbance in the vasculo-connective tissue stroma of the neoplasm. The above experiments indicate that daily treatment at low intensities over a period of from one to two hours is preferable to daily treatment of a few moments with high intensities, because the effects upon radiosensitive epithelial cells does not vary with intensity whereas the severity of reaction in the stroma is less with low intensity irradiation.

TABLE II

Patient	A. R., 65 yrs. (129,594)		A. L., 65 yrs. (130,822)		O. A., 45 yrs. (132,357)		P. G., 52 yrs. (102,922)		B. B., 45 yrs. (124,367)	
	Rt. thigh	Left thigh	Rt. thigh	Left thigh	Rt. thigh	Left thigh	Rt. thigh	Left thigh	Rt. thigh	Left thigh
Dose	636 r		636 r		626 r		600 r		600 r	
Time	124 min.	6 min. 50 sec.	5 min.	96 min. 35 sec.	104 min.	5 min. 35 sec.	84 min.	4 min. 48 sec.	84 min.	4 min. 48 sec.
Ratio	18:1		1:17		18+1		18+1		18+1	
Erythema	faint	+++	faint	++	faint	+++	+	++	very faint	+

The erythema reactions recorded were observed from three to four weeks following irradiation.

Furthermore, the difference in reaction to variation in intensity of irradiation, exhibited on the one hand by epithelium (germinal epithelium of testes) and on the other hand by vasculo-connective tissue both *in situ*, suggests that the roentgenotherapeutic problem of carcinomas is a question apart from that of sarcomas.

SUMMARY AND CONCLUSION

(1) Experimental studies are presented to show that:

(a) Variations in intensity (1:17) of a given quantity of irradiation produced no variation in the reaction of non-neoplastic radiosensitive epithelium (rat testes) *in situ*.

(b) Variations in intensity (1:18) of a given quantity of irradiation produced variation in the intensity of non-neoplastic mesoblastic tissue reaction *in situ* (erythema in human skin). The higher intensities produced the more marked reactions.

(2) A difference in sensitivity between non-neoplastic epithelial tissue and non-neoplastic mesoblastic tissue both *in situ* to variations in intensity of irradiation suggests a fundamental difference in the roentgenotherapeutic problem of carcinoma and sarcoma.

(3) The experiments reported are interpreted as evidence favoring the prolongation (low intensity) of daily exposures in the treatment of carcinoma, since by such irradiation the likelihood of undesirable excess reaction in the vasculo-connective tissue stroma in and about the neoplasm is reduced, while the effects upon the radiosensitive epithelial cells (carcinoma) are equal to those obtained by irradiation at a high intensity.

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DISCUSSION OF SYMPOSIUM

DR. R. L. SCHAEFER (Detroit): We have listened to an excellent symposium, and I want to compliment the essayists on their presentations. The limitation of time precludes any detailed discussion of the specific papers.

Dr. Collip has given you an interesting review of the advances that have been made in the endocrine field in the last few years. He, personally, has contributed much. Despite the advances that have been made, the gospel of endocrine medicine has been slow to spread amongst the general profession. No group has been more laggard than the radiologists. This is in no way an indictment of either the general profession or the radiologists.

Dr. Hodges' reference to Dr. Barger belittling much of the effort along clinical lines is only partly true. There are two factors which certainly do prevent and have prevented the dissemination of knowledge. The first, as pointed out to you, is the unwarranted claims of the detail men representing unscrupulous pharmaceutical houses. The second is the perverse stand of the tradition-bound faculty member toward this new branch of medicine. If this subject were permitted to be established in its proper place in the curriculum of the medical schools, it would allow the oncoming members of our profession to think for themselves, to diagnose and treat intelligently their endocrine patients.

There are three papers which are of special significance to the radiologist: Dr. Hodges', Dr. Shepardson's, and Dr. Mortimer's.¹ The x-ray is an essential mechanistic procedure in the diagnosis of hyperparathyroidism, hypothyroidism, and hypo- and hypergonadal disturbances. The roentgen diagnosis of hyperparathyroidism has been fully covered by Dr. Hodges.

¹Not received for publication.

Dr. Shepardson's paper deals with the roentgenographic study of osseous development, which was developed by Dr. William Engelbach. Briefly, a delay in time of appearance of the various osseous centers is significant of a hypothyroid disturbance. A delay in epiphyseal closure signifies hypogonadism. In the hypergonadal type of individual we see the inverse, or an early epiphyseal closure.

The studies of Dr. Mortimer are most convincing because he has correlated his experimental studies in the rat and has shown us clinical prototypes of his patients presenting various phases of dyspituitarism. Most interesting is the fact that he can predict from his skiagrams approximately at what period in life the pituitary dysfunction occurred.

It would seem advisable that the studies of these men, Engelbach, Mortimer and, also, Todd, should be advanced by the radiologist. He has access to a vast amount of roentgenograms in the pre-adolescent, or formative, years of life. Proper evaluation and correlation of these three forms of roentgenographic study would be a boon to the clinician and would obviate the too frequent reports from the radiologist to the clinician which are usually worded as follows: "The films of your patient reveal no signs of gross endocrine dysfunction." Unquestionably, the roentgenologist can and should play an important part in the development of diagnostic endocrinology.

The field of the radiologist in endocrine therapy is less evident. In general, one can state that specific replacement therapy is preferable to radiation of any specific gland. This is especially true because of the apparent multiplicity of function of the various glands and their inter-relationship. Specifically, then, in the treatment of the menopause I see no necessity for radiating the pituitary if the same therapeutic response can be obtained by replacement of a sufficient amount of the lacking estrogenic substance.

Dr. Steel leaves no method of choice when dealing with malignancy of the breast with or without metastases: radiocastra-

tion is positively indicated. Too, castration is occasionally indicated in other instances, and, in general, radiocastration is to be preferred to surgery. In radiation treatment of a hyperparathyroidism one would first have to be assured that radiation of the neck would not destroy nor upset the function nor the inter-relation of the thyroid.

DR. JAMES H. HUTTON (Chicago): I am not a radiologist. A couple of years ago I had the temerity to announce that I thought that the x-ray might be used in the treatment of essential hypertension and diabetes. While I expected a great deal of criticism from the general profession, I thought the radiologists would sort of take me to their bosom and I would have in them very warm defenders. Nothing of the kind occurred.

They didn't accept my ideas nor accept me, and now I am in the same position as Dr. Collip; I owe my invitation here to the fact that I know Dr. McGuffin.

I notice that Dr. Collip said he was an endocrinologist. I am interested in that. I thought Dr. Collip was a physiologist, and I am wondering if endocrinology has so broadened that Dr. Collip is now a physiologist, which means that he is an endocrinologist.

Every man measures what he sees or hears by the yardstick of his own experience and is impressed by the thing that particularly touches his own work. That has been the case with this program this morning, and inasmuch as time does not permit a general discussion of the very excellent papers that were presented, I should like to point out some things that did particularly interest me.

Dr. Hodges' concluding exhortation applies undoubtedly to research men much more than it does to men who are in clinical medicine. The research men, as I see it, have problems to solve that do not necessarily involve the improvement of the patient's condition. The man in clinical medicine is confronted by a patient who wishes to be relieved and to be kept on the

job, and he doesn't ask the doctor how the latter does it. The clinician is consequently compelled to do a good many things empirically. Later, the research man tells him why his empiricism worked so well.

There is another objection to allowing the experimentalist solely to lead the way, and that is the fact that animal experimentation is not always applicable to clinical practice. A very good example of that occurs in Dr. Hodges' institution.

Dr. Barnes has taken a series of dogs and rendered them totally diabetic by removing their pancreas. After he has stabilized them on diet and insulin, he has taken them over to the Illinois Central Hospital and irradiated the pituitary and adrenals. After these treatments their insulin requirement dropped 50 per cent. This occurs quite regularly and the results with one pair of dogs are exactly comparable to the results with every other pair.

No such regularity occurs in our clinical experience. It is true that in a good many cases of diabetes, symptoms, hyperglycemia, and glycosuria disappear quite promptly. This has been so for two or three years, but it doesn't occur with the regularity that Barnes observes in his dogs. And yet he knows that he has a real pancreatic diabetes. In my opinion we don't often see that in the human animal.

I was interested particularly in what Dr. Collip said about the effects of large and small doses of parathyroid hormone: apparently, diametrically opposite effects are observed. In treating hypertension we find that the patients are relieved—their blood pressure in about 75 per cent of cases is markedly reduced by what we call very small doses, meaning about 120 kv., three to five milliamperes, delivering about 50 r units. If we give larger doses, 180 to 200 kv., delivering above 100 r units, we do not relieve their symptoms. The patient usually feels worse, has headache, vertigo, weakness, and nausea. These large doses have no effect at all on the blood pressure.

Dr. Mortimer suggested that we either disregard the sella or view it in relation to

the whole skull. For a good many years I was convinced that in studying clinical pituitary disorders the sella gave us very little information.

Since we have been studying hypertension, we are convinced that we get from that some idea as to whether or not that patient is likely to experience relief following irradiation. If the sella is large and there is some excess of calcium about it, we think his chances are very good. If it is quite small, we think they are not nearly so good.

I was interested in Dr. Menville's paper because he said headache was one of the things not relieved, as a rule, by irradiation. Our experience in hypertension is that headache is one of the symptoms most promptly relieved, but it is done by very small doses. Vertigo is perhaps relieved a little more promptly. But a sense of well-being, a loss of nervousness and irritability, a sense of tranquillity are things that occur very promptly and I should say in 90 per cent of the cases.

I have been interested in the discussion of super-voltage. Knowing something about voltage and what "super" meant, I gathered that the radiologists felt as most of the human race do—that if a little was good, more was better, and consequently they were using larger and larger voltages or, in the words of the clinician, doses. I believe we make many mistakes in following this idea.

I want to conclude by saying that I have enjoyed this very much and I have this criticism to offer of the radiologists. You can do a great many things by irradiation that are very valuable to the patient and would be almost as valuable to the clinician if he knew about them. Some years ago a newspaper editor said that among all the noisy inhabitants of this country there was a large group of medical men that were very silent. It seems to me that of all the medical men the radiologists are the most silent, and this to the disadvantage of the rest of the medical profession.

DR. MILTON FRIEDMAN (New York

City): Concerning Dr. Menville's paper on the irradiation of the pituitary glands in an attempt to eradicate the symptoms of menopause, there seem to be several impressions as to exactly what gland is primarily responsible for the symptoms of menopause. Actually, we do not know what initiates menopause, but the impression of some is that the ovary is primarily affected. This is confirmed by histologic and quantitative hormone studies.

When the ovary dies, the anterior pituitary gland, being the motivating factor, attempts to compensate by secreting an excessive amount of prolactin in order to whip up the lagging ovary. Consequently it would seem to be injudicious, theoretically, to irradiate the pituitary in an attempt to alleviate symptoms produced primarily by the ovary, especially since it is actively engaged in postponing the climacteric.

The question then arises: Does the pituitary gland, during this period of compensatory hyperactivity, produce the symptoms of menopause? In seeking the answer in analogous instances, we come across cases such as this: a woman beyond the age of menopause developed a pituitary adenoma not producing severe symptoms since it was in an early stage. Quantitative hormone assay revealed tremendous quantities of prolactin. This would indicate a functioning hyperplastic adenoma. Irradiation of that gland caused an alleviation of the headaches and vertigo. However, that woman had no hot flushes, no nervous instability or any other symptoms referable to the menopause, although there was an undoubted pituitary hyperplasia and hyperfunction.

Another case is that of a primary gonadal deficiency in a young woman who menstruated scantily at first, and then developed secondary amenorrhea. In making quantitative hormone assays over a period of time, we found at first a fairly normal prolactin during the menstruating phase. When ovarian secretion diminished and amenorrhea set in, there resulted a gradual rise in the prolactin as the pituitary gland commenced to compensate. In this young

girl we finally found the same picture as seen during menopause—tremendously high quantities of prolactin secretion. However, there were no symptoms of menopause such as nervous instability, headache, and vasomotor phenomena. Heavy irradiation of her pituitary gland, tried experimentally, was useless. The prolactin was brought down only by the subsequent administration of estrin.

These are clinical experimentations. There has been considerable laboratory work done on animals which substantiates this thesis.

As the first discussant pointed out, the administration of estrin, which is certainly a simple and conservative measure, is attended by a very high number of successes. It is our impression that in cases in which the administration of estrin fails, x-ray therapy will also fail, and that there is a basic psychoneurotic disturbance with exaggeration of the symptoms which is primarily responsible for the complaints of the particular patient. Therefore, in our attempt to disseminate the use of radiotherapy in endocrine disturbances, it might be a bit injudicious to state that we should irradiate the pituitary gland of women who are suffering from excessive symptoms of menopause.

With reference to Dr. Steel's paper, once again a word of caution is suggested. There seems to be no doubt on the basis of the few though indisputable cases reported, that roentgen castration of the ovaries will cause a temporary disappearance of metastatic lesions in the bone.

However, can we advocate this relatively radical procedure—radical in the eyes of the surgeons as well as of patients—for all cases of carcinoma of the breast? There are some clinical and theoretical reasons why roentgen castration may not help all cases of carcinoma of the breast. Firstly, cancer of the breast occurs most commonly around the age of 50, when Nature has already curtailed the production of the ovarian hormones, a fact which interdicts the ovary as an important contributory etiological factor. Secondly, most carci-

nomas arise on the basis of long-standing mastopathies, some of which are corrected by the administration of estrin. Furthermore, in the study of the benign breast hyperplasias, it has been shown that large quantities of estrin cause a dilatation of the ducts only. We have analyzed several cases of diffuse duct carcinoma of the breast. The lining cells of these ducts have undergone a transposition involution to malignancy, but still retain their differentiated ductal architecture. In certain of these pathologically clear-cut cases, there was found a deficiency of the ovarian hormone secretion with a compensatory high rise in the prolactin secretion. One would expect a high estrin with a duct carcinoma. In spite of these considerations, I still propose to castrate patients with carcinoma of the breast whenever possible, until the indications for this procedure can be more accurately delineated.

Experimentally it has not been demonstrated that the administration of large quantities of hormones will produce carcinoma of the breast. Lacassagne's work is frequently quoted to prove that he produced a high incidence of carcinoma by the administration of the ovarian hormone. What he actually did in a strain of mice normally susceptible to 72 per cent spontaneous carcinoma of the breast, was to give estrin to the male mice of this strain so as to develop their breasts to a female maturity and thus permit their hereditary tendency to cancer to exert itself. He specifically did not produce carcinoma of the breast by the administration of large quantities of estrin.

Dr. Brunschwig's presentation is a valuable contribution to the study of the relation of the time intensity factor to the rhythms of radiation effect and tumor response. However, we have found it impossible to apply these studies based on single incident doses to protracted, repeated-dose irradiation. For instance, one of his studies compares the radiation administered over a period of one-half hour with that of two hours. This is an apparent time ratio of 4 to 1. In protracted irradiation,

however, the factor of daily recovery must be considered. Consequently, on the one hand, the cells are resting for a period of twenty-three and a half hours, and on the other hand, for a period of twenty-two hours. This is actually not as great a difference in the time intensity factor as originally implied. Most current time intensity tests do not consider the influence of this recovery time, which becomes magnified when the treatments are given over a period of from three to four weeks. It overshadows the importance of the exposure time. A daily treatment time ratio of one hour of exposure compared with twenty-four hours exposure, when protracted over a period of from twenty to thirty days, will show only a variation in erythema intensity of 4 as compared with 5.

In trying to make some practical application of that, I think we might say that, where economics must be considered, it is feasible to use the high milliamperage and give the treatment over a short period of time, providing we split the rest period, giving one treatment early in the morning and the other late in the afternoon.

PAUL S. HENSHAW (New York City): I should like to discuss one point in connection with Dr. Brunschwig's paper on the time factor.

If I have followed correctly, Dr. Brunschwig selected two biological responses to radiation—the production of the skin erythema in one case and the destruction of germinal epithelium of the testes in the other—and has exposed the test materials to radiations varying in intensity as much as 1 to 18. In case of the erythema a greater effect was obtained when a high intensity and short exposure was used; whereas, in case of the germinal epithelium, about the same effect was observed irrespective of whether a high intensity and short exposure or a low intensity and long exposure was used. Thus, a time factor effect was found in the first case but not in the second.

On the basis of this it was suggested that if tumor tissues respond to radiation as did

the germinal epithelium, clinical advantage would be obtained by using protracted radiation. This raises a question in regard to treatment economy. A manufacturer of x-ray equipment has mentioned to me that since the recent visit of Coutard to this country, there has been a rather general tendency on the part of those purchasing apparatus to want to give protracted treatments. The manufacturer pointed out that if low intensity radiation is what is needed, much less expensive equipment can be used to supply it.

At the morning session we were privileged to hear reports dealing with recovery from x-ray effects in the human skin. It was pointed out that recuperation takes place rapidly following exposure and that it takes place even during treatment. Thus, we can see a reason why the skin is affected relatively less when protracted treatments are used. Moreover, it is obvious that the same advantage may be obtained by administering high intensities and using the divided dose technic with proper doses and spacings. Thus, the advantages of protracted irradiation alluded to by Dr. Brunschwig should be obtainable, even when high intensities are used, and thereby eliminate the disadvantages which go along with long treatments.

DR. MERRILL C. SOSMAN (Boston): In view of what Dr. Hutton said about having a patient on your hands who desires and demands clinical relief no matter how obtained, may I add a clinical observation in the cases Dr. Steel referred to? This observation may be of some benefit to you, as it has been to me.

In a patient who has carcinoma of the breast with skeletal metastases, the pain may be considerably exaggerated during the menstrual period. If you get this information from your patient, then you can practically promise her considerable relief by artificial menopause. This is a very striking coincidence and is probably due to hormonal influence from the ovary upon the breast tissue which is forming the metastases.

I might also add that we are producing artificial menopause with x-ray treatments in all women with carcinoma of the breast who are still menstruating, regardless of whether or not they have metastases. This same principle is in force at the Massachusetts General Hospital and the Collis P. Huntington Memorial Hospital.

In addition to relieving the patient of her pain, if she has metastases, there is a very important secondary benefit from artificial menopause, namely, the patient is prevented from becoming pregnant. As you all know, pregnancy very often stirs up cancer so that it spreads like wildfire.

In view of these findings, I think we should all seriously consider routine roentgen castration of all women with cancer of the breast who are in the pre-menopausal period of life.

DR. ALEXANDER BRUNSCHWIG (closing): I am sorry that I did not make myself clear in regard to conclusions concerning long and short treatment periods. I did not mean to imply that we were definitely committed to prolongation of individual treatments, as I believe Dr. Henshaw interpreted what we said as implying.

I do not think we know, and I do not think anyone knows, which is superior at the present time if, indeed, there is any difference. It is true that Coutard developed his technic with apparatus that could operate only at low intensities. As far as I know, he does not have a large series of cases treated at 25 milliamperes to compare with his original series treated at three, four, and five milliamperes.

Our studies were merely attempts to find evidence as to which type of treatment we should use. Whereas we hesitate to draw conclusions on the basis of what we have done, we cannot help but feel (and this is purely personal) that if it be true that better results are to be expected in cases in which the stroma of the tumor is less affected than in cases in which the irradiation is given in such manner that there is a violent vascular reaction, irradiation should be administered at low intensities. This is

not a new reason for favoring low intensity irradiation. We simply present our experimental results which we interpret as additional evidence favoring low intensity irradiation in the treatment of malignant epithelial neoplasms.

We feel that if we got these reactions with 600 r, that in giving 250 or 300 r a day, even though it might not be so apparent, the vascular disturbance in the stroma of an epithelial tumor is less in cases in which there is protraction of individual treatments than in cases in which short, high intensity treatments are given.

With 25 milliamperes and 0.5 millimeter of copper filtration, about 200 r (measured in air) are delivered by our tubes in from eight to eleven minutes, and using the true Coutard technic it takes anywhere from two to two and a half hours, so that the time ratios are approximately the same between high and low intensity treatments as in our experimental observations with high and low intensity exposures.

DR. PAUL C. HODGES (closing): Dr. Newell² has described a splendid example of the type of experimental controls that Dr. Barger has been urging upon us. At first thought one wonders why others have not controlled their experiments the way

Dr. Newell has done. The answer is probably as follows:

In Dr. Newell's cases the dose was so small that there was no visible skin effect and as a result Dr. Newell was completely unbiased as he conducted his physical examination of these patients. There was no surface indication to differentiate treated cases from untreated cases.

Controlled experiments on the effect of testicular extract are not so easily arranged. Professor Moore, of the University of Chicago, who is working on testicular extract, has confined his work to animals so that he can weigh the tissues concerned. In human experiments of this sort the evidence must rest largely on changes in secondary sex characteristics. Judgment as to these changes takes us into the field of psychology and makes it extremely difficult, if not impossible, to establish genuine controls.

DR. DAVID STEEL (closing): I would simply like to thank Dr. Sosman for the very important point he brought up in connection with my paper. It is a point that I did not know and I think adds materially to what I had to say.

Dr. Mortimer spoke of urgency in some of these cases. Certainly in cases that fall in the group of which I talked there is this urgency, and we are very fortunate indeed as roentgenologists and radiologists to have such a simple method at our disposal.

² See Effect of Irradiation of the Pituitary in Dysmenorrhea, by R. R. Newell and A. V. Pettit, *RADIOLOGY*, October, 1935, 25, 424-428.

ACUTE PAINFUL ANKYLOSING ARTHRITIS

WITH ESPECIAL REFERENCE TO THE NON-SUPPURATIVE TYPE

By HARRY A. OLIN, M.D., *Chicago*

From the X-ray Department, Woodlawn Hospital, Chicago

THE literature on arthritis is so voluminous that one hesitates to add more material to a subject, the groundwork of which has been covered so exhaustively. Text-books cover the subject exceedingly well, and classifications are numerous and varied. A well directed effort has been made by the International Committee on Rheumatism to study the subject intimately and to report from time to time their findings on

classification. It is not my purpose in this paper to deal with arthritis in general but to confine my remarks to a type that is acute, exceedingly painful, and inevitably terminates in ankylosis.

My apologies are due the reader for these prefacing remarks, but since this form of arthritis is invariably of the dry and non-suppurative type associated with excruciating and agonizing pain, in which early

CLASSIFICATION OF ARTHRITIS, INTERNATIONAL COMMITTEE FOR CONTROL OF RHEUMATISM, OCTOBER, 1930, KANSAS CITY

	Atrophic Arthritis	Hypertrophic Arthritis
Common synonyms	Rheumatoid arthritis	Osteo-arthritis
Terms employed in other classifications	Proliferative or ankylosing arthritis Arthritis deformans "Poker-back" spondylitis rhizomelique— Strümpell-Marie type Still's disease (children)	Degenerative or non-ankylosing arthritis Osteo-arthritis of the spine, von Bechterew's syndrome Malum coxae senilis
Age	From infancy to middle life	From middle life to death
Incidence
Body type	Somewhat more common in slender, ptotic men and women	Somewhat more common in stocky, well nourished men and women
Onset	Acute to insidious	Subacute to symptoms or ignorant of their presence
Symptoms and signs	General health usually not robust; fatigued easily Pain and disability often pronounced Joint swellings and muscle atrophy to be observed	General health usually less disturbed Pain and disability often slight Joint swellings and muscle atrophy less noticeable
Early roentgenologic appearances	No apparent cartilage or bone changes; general increased density of soft parts Diminished density of bone; atrophy; no lipping	Slight lipping of articular margins; no general increased density of soft parts Less diminished density of bone (unless from long non-use)
Late	Narrowed articular space-subluxations; ankylosis	Articular space irregular; hyperostoses; no ankylosis
Early marked histology	Early proliferation of synovial membrane—"pannus" Usually small round-cell infiltration; epithelioid nests	Early fibrillation of articular cartilage; no general proliferation of synovial membrane; no small round-cell infiltration Chondro-osseous hypertrophy of articular margins
Late	Late destructive and atrophic processes in cartilage and bone Fibrous, true, bone ankylosis	Late eburnation; deformation and hypertrophy of articular bone ends; cyst-like cavities in cancellous bone near articular surface; joint mice common No true bone ankylosis

the etiology and best methods of treatment. This Committee has been functioning since 1930 and has created a well laid foundation by simplifying the nomenclature and establishing a simple, concise

roentgenograms are usually negative, the writer will deem it a well-merited effort if he calls attention to it so that an earlier recognition of this crippling condition may be made.

My attention was recently attracted to this form of arthritis by two cases occurring in young women whose pain was so acute that, in order to radiograph them properly, each had to be narcotized before submitting to examination. While much has been written on painful and ankylosing arthritis, the writer has been able to find but little in the text-books or literature on the acute, painful, ankylosing type. As a composite clinical entity, Stern, of Cleveland, has emphasized this condition and cited two cases in a paper read in 1928 before the Orthopedic Section of the American Medical Association in Minneapolis. To quote: "But the combination of symptoms here described is so little known, the sufferings of the patients have been so great, the relief afforded by the proper recognition and treatment has been so striking, and the process has recurred so characteristically in a sufficient number of cases that I am impelled to put my observations on record as a composite clinical entity" (1).

As a perspective of arthritis, here is appended a classification adopted by an international committee.

CAUSES OF ANKYLOSIS¹

Ankylosis is, in the first place, a secondary condition, and is invariably the result of a previously existing disease either local in or about the joint, constitutional, or general. Theoretically, congenital ankylosis may occur, but the writer has been unable to find reference to it in the literature. If ankylosis does occur in a joint, it is invariably the end-result of a reparative process.

The causes may be classified as follows:

- (A) 1. Injury of articular surfaces, penetrating and puncture wounds.
2. Fracture into a joint.
3. Non-suppurative inflammatory joints involving the formation of fibrous adhesions, or contraction of ligaments, whether

traumatic, rheumatic, gouty, gonorrheal, tuberculosis, etc.

4. Pyogenic infections.

5. Destruction of bones, whether or not it is associated with articular disease, as in Pott's disease of the spine, typhoid osteomyelitis, malignancy involving the joint followed by repair, and osteomyelitis invading the joint, tumors destroying the joint, etc.

(B) Nervous diseases leading to a chronic form of arthritis. Lesions may be central as in the spina bifida, tabes, syringomyelia, or peripheral, as in neuritis, Raynaud's disease, diabetes, leprosy, or division of nerves.

(C) Long-continued abnormal pressure of contiguous bones may result in ankylosis, as in scoliosis or arthritis deformans of the spine. In the latter disease, immobility may be due either to ossification of ligaments or to the interlocking of osteophytes.

Ankylosing arthritis may involve any joint in the body and forms one of the common sequels of some types of arthritides. Perhaps it may be well briefly to review some of these well-recognized clinical types before describing the acute ankylosing entity.

SPINE

Perhaps von Bechterew's chronic spondylitis which he first described in 1893 is the best example. It consists of a progressive stiffening of the spine, which, beginning in the dorsal region, extends downward and becomes associated with marked kyphosis. Clinically, there are signs and symptoms of nerve involvement, namely, paralysis and atrophy of the muscles of the back, especially in the upper portions in which diminished sensitivity and psychic phenomena are present. The x-ray signs in advanced cases show a well-rounded dorsal kyphosis, with anterior narrowing of the vertebral bodies fused at their anterior margins, marked atrophy of the discs with much deposit of calcium in the cartilages, and calcification in the paraspinal ligaments.

Strümpell, in 1897, and Marie, in 1898,

¹ In the main taken from the text-book of Rose and Carless, *Manual of Surgery*, eighth ed., p. 675. William Wood & Co., New York, 1912.

described somewhat different forms of ankylosing arthritis in which the process first began in the lower spine and progressed dorsalward. The main roentgen findings consisted of the sacro-iliac joints obliterated by firm bony ankylosis. The vertebrae showed no changes in form but a general demineralization. The discs were normal in width but acquired an osseous character. The paraspinal ligaments became ossified, enclosing the vertebrae in a thin bony sheath for the entire column. The usual involvement of the hips and shoulders in the ankylosing process led Marie to designate the affection as "spondylose rhizomelique." Knaggs classified the Marie-Strümpell type of spondylitis as "spondylitis ossificans ligamentosa," believing that the ossification in the ligaments was the most important change. Marie considered this ankylosing type of spondylitis not directly infectious, but probably of toxic origin, and indicated the possibility of a nutritional basis for the disease (2).

Ankylosing spondylitis is sometimes also seen following trauma, pyogenic or suppurative arthritis, and occasionally as an end-result of healed tuberculosis. Such ankylosis is the terminal process of a long chronic joint involvement which may require from six months to two or more years to produce fixation. The more common arthritides which may lead to permanent ankylosis may be mentioned: the pyogenic, rheumatoid, gonorrheal, traumatic, and tuberculous.

PYOGENIC

It is well known that local suppurative conditions such as osteomyelitis or suppurative systemic infections from any local source, may lead to a joint infection with bony ankylosis as an end-result. Several authors in their classification have included acute infectious monarticular arthritis secondary to streptococcus or staphylococcus invasion elsewhere, such as boils, carbuncles, colds, sinusitis, tonsilitis, etc., in which the end-result is either complete restoration of the joint with complete function, or a completely destroyed joint with

firm bony ankylosis, or a loose unstable joint (3).

In 217 cases of pyogenic osteomyelitis reported by Bisgard (4), there was an associated arthritis in 51 cases, an incidence of 23.5 per cent. This author, in analyzing the joint involvement, found 42 cases resulting from direct extension from the adjacent diaphyseal infection, the large weight-bearing joints forming 92.5 per cent of this group. The other nine cases were from a blood stream infection. The hematogenous group showed less joint damage, although the percentage of ankylosis was 44.5, whereas a good range of motion was preserved in 33.3 per cent. In this group the joints involved were the temporomandibular (3 cases), the hip, the knee, and the elbow (each in 2 cases). All three temporomandibular cases subsided without drainage.

The joints involved with respect to the bones from which extension occurred were as follows:

	Instances
Knee (19 cases: 36 per cent)	
Distal end of femur.....	13
Proximal tibia.....	6
Hip (14 cases: 26.4 per cent)	
Proximal femur.....	10
Ilium.....	4
Ankle (12 cases: 22.6 per cent)	
Distal tibia.....	10
Tarsal bones.....	2
Sacro-iliac (4 cases: 7.5 per cent)	
Ilium.....	4
Shoulder (2 cases: 3.8 per cent)	
Humerus.....	2
Elbow (1 case: 1.9 per cent)	
Humerus.....	1
Wrist (1 case: 1.9 per cent)	
Carpal bones.....	1

Of the entire group of 217 cases of osteomyelitis, the tarsal bones were involved twice, the carpals only once. Extension to adjacent joints occurred in all three cases.

Bisgard's tabulation of end-results in the direct extension and hematogenous groups are as follows:

	Infection by			
	Direct Exten- sion	Per- centage	Metas- tasis	Per- centage
Ankylosis.....	Cases 34	65.2	Cases 4	44.5
Limited motion....	12	22.6	2	22.2
Full range motion..	7	13.2	3	33.3
Total joints.....	53		9	

GONORRHEAL ARTHRITIS IN INFANCY AND CHILDHOOD

Pyogenic arthritis not uncommonly follows local gonorrheal infection, the primary site of the disease occurring in the rectum and vagina. In 53 cases of gonorrheal polyarthritis, Cooperman (5) found eight cases (four males and four females) of hip involvement in the newborn. The blood stream infection came from the local seat of the disease, and the portal of entry was the rectum. In five cases it occurred on the right side and in three on the left. The symptoms were pyemic in nature, with vaginal and rectal discharges. The fluid in the hip joints was purulent, and gonococci were found on smears.

In a second group of six cases of pyogenic arthritis mentioned by the same author, hip involvement followed a suppurative mastoid in two cases, a pyelitis in another, and three in which the portal of entry was undetermined. The ages of the children ranged from five to thirteen years. The hip involvement occurred two and seven days, respectively, after a mastoidectomy, and the third followed 16 days after an acute attack of pyelitis, the latter case showing a positive blood culture with a high white and polymorphonuclear count. Two children who were treated conservatively showed no evidence of disease by roentgen ray. In two cases diagnosed as osteomyelitis of the upper femur, the roentgen ray examination was negative. Both cases were operated upon and drained but the hip joint was not explored. Peri-arthritis developed in both cases, necessitating a resection of the hip in one of the children, and in the other a bony ankylosis developed.

PURULENT ARTHRITIS

Reich has collected 20 cases of purulent arthritis in which 32 joints were involved. Twelve cases had involvement of one joint, five of which were of gonorrheal origin, and eight cases had involvement of three or four joints. Of the Neisserian joints, two resulted in complete ankylosis, one obtained 100 degrees flexion, and the remaining two

had complete restoration of joint function. In gonorrheal arthritic joints the same author regards the knee as the most common site, and next the foot and hand, followed by the fingers and toes. Trauma plays an important part in localization of infection. Purulent arthritis he considers as being more common in children than in adults. From the standpoint of etiology he roughly divides purulent arthritis into three classes (6):

- (1) Blood stream (infecto synovia primarily).
- (2) Penetrating wounds, as compound fracture, gunshot and puncture wounds.
- (3) Acute osteomyelitis which invades diaphysis adjacent to epiphyseal plate

Reich in his summary contends that good results are obtained when cases are treated early, and that ankylosis follows neglected or mistaken diagnosis, and in cases in which erosion of cartilage has occurred.

Ankylosis following gonorrheal infection, which is usually metastatic, has been mentioned. Although occasionally this form of arthritis may become polyarticular in type, as a rule it is distinguished by its monarticular character.

Caldwell, in a study of 17 children in whom 18 hip joints were involved, obtained the following end-results: eight hips were normal and nine had ankylosis or a very small range of motion. He concluded that ankylosis or pathologic dislocation is the usual sequel when the primary site of infection is in the intra-articular bony structures, whereas excellent functional result is the rule when the process begins in the synovial membrane. All of his children were under fourteen years of age, and 13 of them were under six. He includes the following conditions named by other writers as part of the same process, notably acute suppurative conditions of the hip (7).

- (1) Acute infectious arthritis (8);
- (2) Acute purulent arthritis (6);
- (3) Acute epiphysitis, upper end of femur (9);

- (4) Acute pyogenic arthritis (10);
- (5) Septic joints (11).

RHEUMATOID ARTHRITIS

Ankylosis is most common in rheumatoid arthritis in the atrophic form, a disease of young adult and middle life. In its early stages it is characterized by proliferative changes in the synovial membrane and by the formation of villi, fringes or tags, hence the name given by Nichols, and in its later stages by erosion of cartilage and atrophy of both bone and cartilage. These latter changes inevitably lead to deformity and ankylosis.

TUBERCULOUS ARTHRITIS

Tuberculous arthritis commonly terminates in the complete destruction of a joint unless, in the unusual event, the disease is conquered before it gains a firm foothold. The destructive stage of the process is so long drawn out that in the attempt of reparation, there occurs partial ankylosis or very rarely true bony ankylosis, particularly if secondary invasion takes place; whereas if ankylosis in pyogenic arthritis does occur, it is invariably of the firm solid type. A tuberculous joint, when secondarily infected, loses many of its characteristics, yet isolated remains may be found here and there and at times it may be difficult to find specific lesions, although the joint is tuberculous (12).

TRAUMATIC ARTHRITIS

Perhaps it may be well to mention traumatic arthritis in a few words. Ankylosis occasionally follows traumatic arthritis, especially when the amount of damage is so great to the articular surfaces and secondary infection involves the articular cartilage. Imperfectly healed fractures, when altering the plane of articular surfaces, may sometimes cause by their chronic irritation changes which may lead to ankylosis.

ACUTE PAINFUL ANKYLOSING ARTHRITIS

This entity so closely resembles acute infectious arthritis that it may be worth while

briefly to review the latter and compare its differences. Both are essentially a disease of young life although occasionally it may be present in individuals past forty. From the etiologic point of view, varied bacteria have been found in the infectious type, whereas none has been found in the ankylosing type; the process in both is invariably metastatic. The most common etiologic factor is some primary focus, usually the tonsils and teeth, single or in combination. The throat also can be considered a very great common primary focus of infection. Next in order can be mentioned the sinuses, gall bladder, colon, and even the cervix may harbor foci of infection.

Stern cites two cases: one in a physician beyond the age of 50 years, who was affected with generalized skin affection and multiple subcutaneous abscesses. The skin lesions healed but on the third day severe, excruciating pain began in the hip joint which, on repeated aspiration, yielded several drops of blood-stained synovial fluid, negative to aerobic and anaerobic cultures. The hip joint was not swollen and there was no unusual rise in temperature. Roentgenograms were negative. Careful palpation did not reveal any localized areas other than a generalized tenderness. Ten weeks following, ankylosis of the hip developed. A roentgenogram at this time showed complete absorption of the joint cartilages and narrowing of the joint space. No evidence of bone destruction or periosteal proliferation was seen.

The other case is that of a woman 23 years of age who developed involvement of the knee following a severe attack of follicular tonsillitis. She had prodromal pains in the legs while recovering from the tonsillitis. Her physician, believing that the leg pains were secondary, hospitalized his patient for a tonsillectomy. Four or five days following the operation, severe, agonizing pain, excruciating in type, developed in the knee, so much so that the slightest jar in bed or motion aggravated the pain. Roentgenograms of the knee were negative. Aspiration of the knee joint yielded

no free fluid; the rise in temperature was slight. Culture and bacteriologic examinations were negative following a second joint aspiration. Swabs made from urethra, vagina, and cervix by a competent gynecologist and cultures by a good bacteriologist, and repeated later, were negative for gonococci. Clinically, the knee at a later date became ankylosed. Subsequent roentgenograms three months later showed complete disappearance of the articular cartilages with no areas of bone destruction or localized periostitis.

Infectious arthritis is usually polyarticular, whereas acute ankylosing arthritis is monarticular; in the former the joints are swollen, tender, and hot, while in the latter, the joints are rarely swollen. In infectious arthritis, fluid is usually increased and may be purulent, while in acute ankylosing arthritis little or no fluid may be found, and, if present, is never purulent.

SYMPTOMATOLOGY OF ACUTE ANKYLOSING ARTHRITIS

There is usually a history of acute, sharp, agonizing pain in the affected joint, all out of proportion to the other clinical manifestations. If the history is carefully obtained, usually some antecedent infection is discovered by the inquirer. Other major joints may be complained of, and even pain along the muscles of a limb, like the thigh or leg, if the hip joint is involved. With active or passive motion, pain becomes intolerable, the patient actually shrieking with it. In the early stage the pain may be migratory from joint to joint, making it difficult for the examiner to determine the joint affected. This pain may continue for several or more weeks until it finally settles in the affected joint. The symptoms are entirely subjective and one is puzzled at the beginning to determine the exact joint involved.

Reich (6) mentions this form of ankylosing arthritis that closely resembles rheumatic fever from which it must be differentiated. There is usually a history of rapidly developing pain in a joint, together with local signs of heat, rigidity, limitation

of motion, and possibly effusion. Soon after, the patient complains of pain in other joints which is less severe and less definite in the local findings. The pains in the other joints soon subside but the original joint becomes more involved, limitation follows, and then ankylosis with severe deformity. He cites the case of a woman, aged 39 years, who, three weeks after an attack of influenza, developed involvement of the metacarpo-phalangeal joint of the left index finger, with subsequent complete ankylosis. She complained of severe pain in her left index finger, her other hand, elbows, shoulders, and left hip. All the joint pains subsided except that of the index finger (metacarpo-phalangeal), which persisted. The joint was hot, swollen, and severely tender to touch, being increasingly painful on motion. Temperature was 103 degrees; white blood count was 15,400. X-ray examination showed a narrowing of the joint space with destruction of cartilage.

In the author's two cases the hip and elbow joints were involved. In the elbow case, roentgenograms taken on the day of admission revealed a normal joint space. The periosteum of the external condyle of the humerus was slightly raised but the cortex and medulla were normal. Three days later the same appearance was seen. The patient then left the hospital, to be readmitted three weeks later. A roentgenogram made on Sept. 7, 1934, showed increasing destruction of the cortex of the internal condyle with the periosteum thicker. Ten days later the joint cartilage presented early destruction with some narrowing of the joint space. On Sept. 24, 1934, the joint cartilage revealed greater destruction with greater irregularity of the articular cortex. The author's case is presented in detail in the appended reports. The subsequent course and study predicted an inevitable ankylosis.

In the hip case, extreme, excruciating pain was experienced in the affected joint although the patient suffered pain in the remainder of the right lower extremity to a lesser degree. For a period of five or more weeks the patient experienced intolerable,

agonizing pain, necessitating frequent administration of morphine to keep her in fair comfort. In the interim, roentgenograms of the entire right lower extremity on two occasions were negative; the third, however, revealed early necrosis of the neck of the femur on the outer side at the base in a circular area about 1.5 centimeters in diameter. Complete details of this case are also appended in the report of Case 2.

PATHOLOGY

What the true etiology of this form of arthritis is still remains unknown. Little or no joint fluid occurs and it is possible from a study and review of these two cases that bacterial emboli in the blood stream are deposited in a terminal vessel or vessels in the periosteum of the metaphysis. The irritation of the periosteum followed by an inflammatory reaction raises this structure and then the process attacks the adjacent articular cortex. Finally, the articular cartilage is invaded and destroyed, producing as an end-result destruction of the joint itself, with ankylosis as a terminal reparative factor. The roentgenograms of both of these cases, especially that of the elbow, support these sequence of events. There is no doubt but what the effect of contact and pressure aid in destroying the articular cartilage in the region of contact of opposing articular cartilages (10). Several cultures from the elbow on aspiration yielded no growth.

DIAGNOSIS

The diagnosis is rather perplexing at first and must be made by exclusion. Early tuberculosis may simulate this condition, although the usual bone atrophy is not present as in caries sicca. Free fluid in the joint was absent in these reported cases as well as those of the author. Bacterial cultures on several occasions in the elbow joint yielded no growth. The dry form of gonorrheal arthritis is another possibility which may resemble this condition, but evidence of Neisser's infection may be obtained both from local examination and from his-

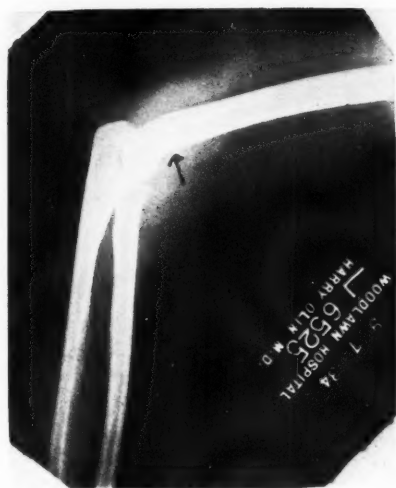


Fig. 1. Case 1. Roentgenogram taken on Sept. 7, 1934. Note destruction of periosteum at the point indicated by the arrow.

tory of exposure in most instances. Besides, in a gonorrheal joint there are usually definite signs of swelling and free fluid. The other types of purulent arthritis even in the mild form will yield, on aspiration, a cloudy fluid with bacteria present from which the culture will corroborate the findings. Rheumatic arthritis generally responds to large doses of salicylates which acute ankylosing arthritis fails to do. *The migratory character of the joint pains finally subsiding in all but the affected joint is the characteristic subjective sign which is the clinical keynote of diagnosis.* Later, the roentgenograms will disclose a narrowing of the joint space, with irregularity of the articular surfaces. Prior to these changes, if persistent roentgenographic examination is made before the application of a plaster cast, early bone destruction will be found, as noted in the hip and elbow cases of the author. Finally, in the course of several months, roentgenograms will disclose complete ankylosis of the joint, always mon-articular. As a rule in infectious arthritis, ankylosis does not occur until after the second or third year (13).

ROENTGEN FINDINGS

Early roentgenograms are always nega-

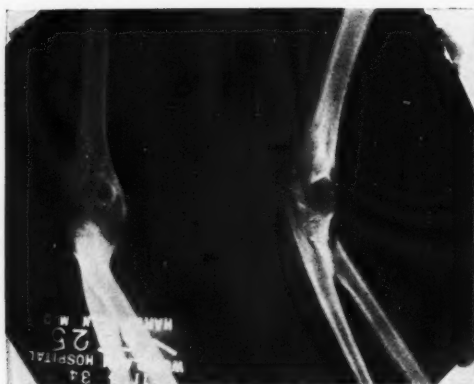


Fig. 2.

Fig. 2. Case 1. Roentgenogram taken on Nov. 14, 1934. Note severe destruction of joint structures, cartilage, and articular cortex.

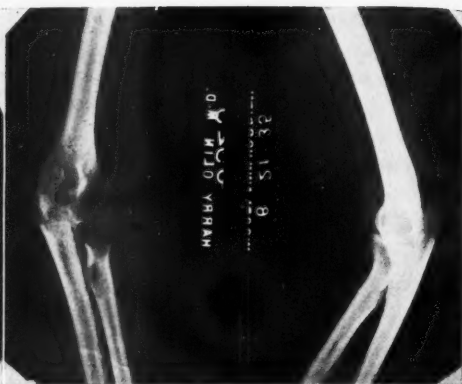


Fig. 3.

Fig. 3. Case 1. Roentgenogram taken on June 21, 1935. Note complete ankylosis of the elbow, especially the ulnar involvement.

tive. To secure the best co-operation of the patient, morphine medication is necessary in order to insure good readable plates of diagnostic quality, as the least motion will defeat this purpose. To make certain that other joints are not involved, roentgenograms should be taken simply to rule out possible pathology other than the affected joint. The earliest lesion shows a raising or slight proliferation of the periosteum, followed by absorption of the cortical edge which is thinned out. Then follows invasion or absorption of the articular cortex which soon becomes irregular and slightly ragged. As the process progresses, the articular cortex deepens and shows roughening. The joint space subsequently is narrowed, the articular cartilages are undergoing destruction, and soon nothing but opposing articular cortical surfaces meet; in other words, bone meets bone with no structures intervening. In the hip-joint case, a circular area of bone destruction was found at the base of the neck. If x-ray studies could have been made prior to this, perhaps there might have been demonstrated a similar sequence of involvement of structures to that shown in the elbow joint. Regional bone atrophy always accompanies these joint changes as well as atrophy from disuse.

SUMMARY

Acute, painful ankylosing arthritis is commonly found in young adults. The clinical picture is usually one of an acute onset, characterized by extreme, severe, excruciating, agonizing pain in the affected joint with little or no swelling and aggravated by the slightest active or passive motion. This stage may be preceded by one in which the pains are migratory, all subsiding in a few days or weeks except those in the involved joint. Finally, the process continues, with eventual ankylosis in two or three months. The temperature is usually of a low grade, and leukocytosis, if present, is slight. Early roentgenograms are negative; later the joint shows definite narrowing and destruction of the articular surfaces, changes which may be preceded by early bone destruction and slight periosteal reaction. Finally, early ankylosis of the joint takes place as a reparative process. Repeated roentgenograms are recommended without the plaster cast, if possible, under the influence of narcosis to avoid motion and to insure diagnostic plates of high quality.

My thanks are due to Dr. F. M. Moeller for the clinical material and for the privilege of reporting these two cases, and to

Dr. Philip Lewin who kindly gave me several valuable suggestions.

CASE REPORTS

Case 1. No. 2,741. E. M., female, unmarried, aged 29 years, was admitted to the Woodlawn Hospital on Aug. 27, 1934, to the service of Dr. F. M. Moeller, complaining of a painful swelling of the left arm, of one week's duration.

Onset and Course.—Five weeks previously, the patient had fallen from a bicycle, bruising her left arm, shoulder, and lower leg. Three and one-half weeks before admission she had developed chilly feelings and a sore throat, followed by a period of being "feverish." She went to bed feeling quite weak. The following morning she noticed a swelling the size of a hen's egg in the region of the left tendo achillis, and there was recurrent smarting pain in this region. After two or three days, the swelling disappeared spontaneously. Immediately following, the left upper arm became swollen and tender. The pains became paroxysmal in character, radiating from the wrist to the left eye and ear. Her arm felt quite stiff, with recurrent twinges of pain. The patient gives a history of numerous functional complaints none of which are related to the present condition. She is an extremely active type of individual. She has had much dental work done recently. Her past history was irrelevant.

Physical Examination.—Essentially negative, except for the left arm, which is slightly swollen and very tender to the touch. There is a firm swelling, the size of an almond, over the left tendo achillis which is subcutaneous, not movable. Tendon reflexes are equal and lively. Her sensation to cotton and pin is normal.

A diagnosis of an infection of the left elbow was made, the result of which led to an operation on Aug. 27, 1934. An incision over the external condyle was made and another below it; there was oozing of blood, but no pus. The wound was left open and hot wet dressings applied. The patient was discharged, her left elbow not

having improved. While at home two weeks, the ache in her arm continued. Soon the left hand and wrist became puffy and tender. Three days before this report she became nauseated and vomited a little clear material. The dull ache has increased.

The patient was readmitted on Sept. 17, 1934. Findings were negative except for the left arm which is held stiffly on the pillow. The joint is swollen and very painful on the slightest manipulation. There is no tenderness over any other of the long bones, nor is there stiffness in the other joints.

A second operation was performed on Sept. 25, 1934. A small opening was made over the soft area, but no pus was found. Her arm was manipulated and a splint applied for fixation. On the same day, four pieces of tissue were submitted for microscopy; they showed non-specific inflammatory changes with polymorphonuclear invasion. (Dr. J. T. Kirshbaum, pathologist.)

Blood Picture	Aug. 27	Sept. 17	Sept. 30
Hemoglobin	80%	70%	
White blood cells	11,000	10,450	8,950
Red blood cells	4,110,000	4,820,000	
Differential			
Polymorph. neutro.	82	84	
Polymorph. eosin.	4		
Small lymphocytes	13	16	
Large monocytes	1		

On Sept. 28, 1934, a culture was taken from the patient's elbow, and given 72 hours' incubation; no growth appeared on either agar or dextrose broth.

Consultation Note.—On Sept., 28, 1934, acute hematogenous arthritis of the left elbow developed, of two months' duration; the last x-ray films show regional bone atrophy and narrowing of cartilage space and irregularity of the articular cortex. Earlier x-ray films show periosteal new bone on humeral metaphysis. The organism was undetermined but it must be of the pyogenic group. Because of the joint destruction, ankylosis of a high grade is to be expected and may be complete.

Treatment.—There was immobilization, with the joint gradually being brought to the right-angle in stages. The patient's

arm has been placed in a plaster cast until all symptoms of infection have subsided. She has been advised against active motion as it may stir up infection. If stiffness results it is possible that arthroplasty for mobilization would be advisable in two or three years (Dr. D. B. Phemister).

ROENTGENOGRAMS

That of Aug. 27, 1934, of the left elbow joint, showed the joint space to be normal, and the periosteum over the external condyle to be raised along the margin for a distance of two inches. The cortex and medulla appeared normal. X-ray diagnosis was periostitis, early osteomyelitis to be considered.

In that of Aug. 30, 1934, the periosteum still showed the same appearance; the medullary canal and cortex appeared normal, as well as the joint space. X-ray diagnosis was traumatic periostitis; elbow joint was normal.

On Sept. 7, 1934, the left elbow showed increasing destruction of the cortex on the external condyle of the humerus, with periosteum thicker (Fig. 1).

On Sept. 17, 1934, the bone destruction appeared greater but localized; several more areas of bone absorption were seen in the region of the external condyle. The cartilage had become involved, with irregularity of the articular cortex.

On Sept. 24, 1934, the cortex and periosteum of the external condyle revealed greater involvement. More regional bone atrophy was present, with greater joint cartilage and cortical articular irregularity. X-ray diagnosis was destructive arthritis of the left elbow.

On Oct. 24, 1934, roentgenograms of the teeth revealed the following: upper left jaw, first molar contained three root canals incompletely filled, with a small area of apical absorption (distal root). Upper right jaw, a large cavity in the body of the second molar involving the pulp chamber. Lower left jaw, no pathology. Lower right jaw, no pathology.

On Nov. 14, 1934, roentgenograms of the left elbow showed that the joint changes

were more extensive, in comparison to the examination of Sept. 24, 1934. The joint space was considerably narrowed and irregular, with the articular surfaces uneven and with apparent involvement of the joint cartilages and synovial membrane. Throughout the articular ends the cortex had thinned out, with the trabeculae being indistinct and showing considerable bone absorption. The periosteal action was still present on the anterior aspect of the joint and seemed to be a little greater than in the examination of Sept. 24, 1934.

Summary.—Left elbow, destructive arthritis, with partial disintegration of joint surfaces (Fig. 2).

On Nov. 16, 1935, x-ray examination of the left wrist showed the articular surfaces of the joint to be uneven and blurred, with thinning of the cortex—due to beginning changes in the articular cartilage (?) All bones showed a moderate osteoporosis, probably due to disuse. Roentgen appearance was that of beginning changes in the wrist joint, probably of an infectious (?) type.

Summary.—Infectious (beginning) arthritis. This joint subsequently cleared up and on June 21, 1935, had normal function.

On June 21, 1935, roentgenograms of the left elbow showed complete ankylosis, the joint at an angle of 23 degrees. The patient had had complete ankylosis of the left elbow for the past four or five months. Figure 3 shows the condition of the elbow on June 21, 1935. Undoubtedly the source of infection was the sore throat aggravated by previous injury and probably complicated by dental infection from a decayed tooth.

Case 2. No. 7,050. D. L., female, unmarried, a clerk by occupation, aged 25 years, was admitted to the Woodlawn Hospital on Feb. 25, 1935, in the service of Dr. F. M. Moeller. Her chief complaint was pain in the right leg to the hip of two weeks' duration.

Onset and Course.—The patient consulted her doctor because of dizziness which had been present for the past eight months. Due to overweight she had

dieted, losing 30 pounds in this period. Several weeks before admission she suffered with a sore throat. Several hours later, she

ing to 102° and 103° at two separate intervals about a week apart, gradually returning to a level between 99.4° and 100° for



Fig. 4. Case 2. Roentgenogram taken on March 21, 1935. Note destruction of upper articular cortex, being greatest at the base of the outer neck indicated by arrow.



Fig. 5. Case 2. Roentgenogram taken on Aug. 31, 1935. Note narrowing of joint, with erosion of articular cortex: end-result, ankylosis.

felt severe pain in the right lower extremity from the hip to the ankle, and was unable to move the fingers of the right hand. Later, she suffered with severe pain in her arm from the right elbow to the wrist, and in her leg, for two weeks. The arm pain disappeared but the hip and leg pain was much more severe. The patient described the pain as a continual ache which was very severe at times, being worse at night, and excruciating on the slightest motion.

Past History.—The patient had had mumps in childhood. Her menstrual history, which began at the age of 15, was regular every 28 days, there being a profuse flow for from 5 to 7 days. Other history was of no importance.

Physical Examination.—Essentially negative except for the right lower extremity. There was tenderness along the right lower extremity from the hip to the ankle; the skin color was normal; there was no swelling of the soft tissues. Excruciating pain was elicited on motion of the right limb. Temperature persisted around 100° with several "flare-ups," go-

ing to the period of the first four weeks at the hospital. The pain in the right lower extremity has become increasingly severe and excruciating. The patient has been under morphia with some relief.

Treatment.—March 24, 1935, the patient was given general anesthesia in order to apply a body plaster cast, which embraced the pelvis and the right lower extremity to the toes and downward on the left thigh to the knee. The patient was then placed on a Bradford frame. Since the application of the cast, she has become much more comfortable, with a decided relief of pain. When moved in bed, however, severe pain recurs. She remained in bed resting very comfortably, and was discharged in the plaster cast on April 23, 1935, her condition being improved. The cast was removed on Aug. 30, 1935, the hip presenting an almost complete ankylosis.

Blood picture	Feb. 25	March 12	March 21
Hemoglobin	75%		70%
White blood cells	10,750	8,400	8,250
Red blood cells	4,390,000		4,470,000

Differential			
Polymorph. neutro.	82	74	69
Small lymphocytes	15	22	27
Large monocytes	5	4	4
Urine: negative			
Wassermann: negative			
Kolmer: negative			
Sedimentation test, March 9, 1935: 15 minutes—3.5 millimeters; 30 minutes—7.5 millimeters; 45 minutes—10.4 millimeters.			

ROENTGENOGRAMS

Feb. 25, 1935, pelvis and hip joints, negative.

March 7, 1935, right and left knees, negative.

March 21, 1935, right hip to toes, inclusive, showed a circular area of bone destruction 1.5 cm. in diameter in the neck of the femur to the outer side at the epiphyseal line, also at the margin of the inner circumference of the head. This was the first indication of pathology; the remainder of the lower extremity was negative. For radiographic examination complete morphia narcosis was necessary (Fig. 4).

June 4, 1935, right hip, showed the joint space narrowed, with roughness of cortex on the outer circumference of the head. Much of the bone detail was obscured by the plaster cast.

Aug. 31, 1935, right hip, revealed a marked narrowing of the hip joint space which is irregular and uneven (plaster cast

was removed previous day). The articular cortex showed erosion with much destruction of the joint cartilage. Clinically, the hip presented an almost complete ankylosis although there was about 5 degrees of flexion (Fig. 5).

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ROENTGENOLOGIC AID IN THE "ACUTE ABDOMEN"

WITH SPECIAL REFERENCE TO INTESTINAL OBSTRUCTION

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DESPITE the tremendous advances in attaining a marked decrease in mortality of practically all other acute abdominal catastrophes, that of intestinal obstruction, especially the acute type, remains appallingly high. When one reviews the literature pertaining to intestinal obstruction, the amazing fact is revealed that the mortality from acute intestinal obstruction is practically as great to-day as it was five decades ago. A conservative estimate of the cross-sectional mortality would place the rate at approximately 45 per cent. Immediately, the important question confronts us: Why this terrific mortality? Paradoxically, the answer can be simply stated in the fact that the mortality is, primarily, directly proportional to the duration of the obstruction, which is dependent upon the time of establishment of a diagnosis. It is patent, therefore, that the earlier a diagnosis is arrived at, the less the mortality will be. However, an inherent factor is the difficulty encountered in a clinical diagnosis *per se*, even when the patient has been observed early. In any series of cases, it is apparent that intestinal obstruction, due to strangulated hernia of the external type, is attended with a markedly lower mortality, which in a great measure is related to the speed of diagnosis, for this entity is readily recognized. Probably of greatest importance is the fact that the commonly accepted criteria, upon which a diagnosis of intestinal obstruction is formulated, are either insufficient or not manifest enough during the early period of the obstruction to even suggest the nature of the condition. Although pain, nausea and vomiting, abdominal distention of meteorism, and obstipation and collapse are present at some time during the course of the catastrophe, it is the procrastination

in waiting for these signs and symptoms to establish a diagnosis of intestinal obstruction that is probably the greatest single factor in losing the most propitious time in which efficient surgical intervention or medical treatment could be instituted.

After it has been repeatedly shown that the mortality of intestinal obstruction, when the diagnosis was made within six hours, is *nil*, and in the first 12 hours is less than 5 per cent as contrasted to 11 per cent for the 24-hour period, with an average mortality of 45 per cent, the crying need for earlier diagnosis is evident. Any auxiliary method which will assist is of worth, and should be assiduously and routinely employed.

It is of paramount importance to have a clear understanding of the general nature of acute intra-abdominal lesions, for it must be acknowledged that, notwithstanding all the methods of precision at our command, occasionally it is impossible to obtain any precise knowledge of the location and nature of the lesion until a laparotomy has been performed. On the one hand, it is a grievous error to wait for pathognomonic clinical signs, which will generally postpone treatment until it is of little avail, *viz.*, ruptured peptic ulcer or acute intestinal obstruction. Merely a reasonable suspicion of such an occurrence makes instant abdominal exploration imperative, and, with our present radiologic aid, should rarely be misdiagnosed. On the other hand, unnecessary operations have been done, but with no serious sequelæ, *e.g.*, in renal or lead colic, and tabetic crisis. However, there exists a small group of cases in which an operative procedure turns the balance of the scale in a fatal direction. These non-surgical conditions are as follows: lobar pneumonia, which frequently is ex-

ceedingly difficult to diagnose clinically in young children; acidosis, particularly in diabetics, and cholera, in countries where that is prevalent. It is obvious that the prime consideration is to decide the necessity of operation; accordingly, the possibilities of roentgenology as an additional aid in arriving at an earlier diagnosis and decision in this regard are herewith presented.

In no other phase of medicine does an accurate history aid one as much as in the roentgenologic diagnosis of the "acute abdomen," and a few of its salient features will be commented upon. An exact anamnesis relating to the character of any preceding illness or pain is important. Thus, quantitative dyspepsia, with pain occurring directly after ingestion of food, in gastric ulcer; or from one to two hours *post cibal*, in duodenal ulcer, together with a sudden abdominal catastrophe, well-nigh lends a diagnosis of perforation. Again, indefinite digestive disturbances of a qualitative nature often precede pancreatitis, biliary colic, etc. An important consideration is the sudden rupture of a silent peptic ulcer, or the not infrequent *formes frustes* type of spontaneous closure with absence of acute symptoms. Fortunately these are readily diagnosed roentgenologically. Icterus suggests biliary colic, and inferentially a possible empyema or ruptured gall bladder, intestinal obstruction by biliary calculus and as a precursor of pancreatitis. Difficult, frequent, or painful urination often precedes or is concomitant with renal colic crises. Parenthetically, a history of progressive oliguria, approaching anuria, has often been noted in acute intestinal obstruction, due to the associated vomiting and resultant dehydration. Not infrequently, an intravenous urographic study is requested by the referring physician and pathognomonic evidence of intestinal obstruction or even peritonitis is disclosed.

Although constipation is common in intestinal obstruction, it is foolhardiness to depend upon diagnostic enemas, for it has been conclusively demonstrated, both

anatomically and physiologically, that the bowel distal to the point of obstruction will expel an administered enema with return of gas and feces.

Previous attacks of pain should be analyzed, to determine whether they are of the type due to a displaced kidney or spleen, or a twisted ovarian cyst, or whether they are of the colic type—biliary, renal, or lead colic.

Although appendicitis may have repeated attacks, the fulminating nature of the initial attack usually presents the difficulty in diagnosis. The occupation of the patient, relevant to possible plumbism must be determined. Traumatism, if direct and severe, may cause visceral rupture or precipitate rupture of an extra-uterine pregnancy. In the latter regard the menstrual history is very important.

An increased pulse rate is practically always present in the "acute abdomen," except in that of a colicky nature. A small, wiry pulse suggests peritoneal invasion, whereas a rapid, compressible pulse, together with air hunger, thirst, lowered blood pressure and hemoglobin, are typical of hemorrhage. Changes in the pulse are important, *viz.*, increased rate with falling temperature is of grave significance. Temperature *per se* is of slight value in early diagnosis, for even in the most severe conditions it may be normal. A tendency toward a "pump-handle" septic type of temperature range is suggestive of suppuration in the portal ducts or of portal pyemia. Subnormal temperature may mean collapse or sudden peritoneal invasion.

Vomiting is an important initial symptom, and even though it may accompany any condition of shock, nausea and vomiting in intestinal obstruction are far more reliable diagnostically than pain, especially if they are persistent and increasing. An important fact is that the most severe cases of perforated peptic ulcer are not accompanied by vomiting as a rule. Blood in the vomitus is, of course, significant.

Constipation to some degree is almost always present in acute abdominal lesions

and its significance has been amplified upon heretofore. Diarrhea, with blood and mucus, suggests intussusception or enterocolitis.

Pain is a common denominator, and its character is important. Initial severe pain is present in acute small bowel obstruction whereas it is exceptional in colonic obstruction. A very sudden onset signifies a ruptured viscus, or biliary or renal colic. Premonitory symptoms are noted in intestinal obstruction, strangulated hernia, etc. The location of the pain is significant but unreliable. Intermittent pain is present in various forms of colic, partial and complete intestinal obstruction, and acute intussusception.

Physical signs are not as important as the history and symptomatology in the acute abdomen. However, local tenderness and rigidity are generally indicative of inflammatory involvement, in contradistinction to relief of pain upon pressure in colic. Abdominal distention is not an early sign of intestinal obstruction. Shifting dullness in the flanks is indicative of free peritoneal fluid. Obscured hepatic dullness suggests free peritoneal gas from a ruptured hollow abdominal viscus. Interposition of the hepatic flexure between the diaphragm and liver is not a rarity and may be confused in this regard. There is rarely a palpable tumor, except in acute intussusception. Displaced kidney, spleen, ovarian tumors, or distended gall bladder may be palpable. Rectal and vaginal examinations should be made whenever indicated.

Curiously, acute intestinal obstruction is the only serious acute abdominal disorder in which physical findings are not present early. Deductively, it should be a diagnostic dictum that in the presence of any acute abdominal complaint, accompanied by intermittent colic, nausea, and vomiting, with no physical signs, the probable diagnosis is acute intestinal obstruction, and confirmatory roentgenologic examination is mandatory. It has been experimentally shown that intestinal obstruction without interference with the blood supply of the

affected part presents late physical findings; but fortunately in this type of obstruction, the roentgenologic findings enable one to make an early diagnosis.

In those cases in which roentgenologic examination does not clinch the diagnosis, careful watching of the progress of the case is imperative, for rapid increase of symptoms in the first two hours indicates a visceral lesion and an exploratory laparotomy. One should never wait for increased distention and vomiting to diagnose intestinal obstruction. Steady improvement follows shock without visceral involvement after trauma, but if there is a rising pulse rate, hemorrhage is present. Sudden relief of pain usually indicates passage of a calculus, or, more important, gangrene in intestinal strangulation, or other inflammatory lesion.

There are certain valuable special laboratory examinations the significance of which are cursorily alluded to in the following: A moderate leukocytosis with relative increase in polymorphonuclear cells, suggests an acute infection, well resisted; *viz.*, an appendiceal abscess. Physical examination of the chest is always extremely important for, especially in children, a basal pneumonitis or pleuritis may simulate abdominal disease. The earliest detection of such a complication is, of course, by roentgenography. Cardiac disease, such as coronary thrombosis, not infrequently presents acute abdominal symptoms.

The urine presents valuable information; for crystals, blood, and albumin suggest renal colic; bile pigments—biliary colic; sugar—pancreatitis; indican—acute small intestinal obstruction; Cammidge's crystals—pancreatitis; acetone and diacetic acid—acid intoxication. In regard to acidosis, this syndrome is treacherous, for an exploratory laparotomy under a general anesthetic will frequently terminate fatally. This condition occurs in obese patients and young children, and in diabetics. Blood sugar and CO₂ combining power estimations are helpful aids in forming a diagnosis. Fecal examination may show blood and mucus as found in cholera,

colitis, or in intussusception. Large quantities of fat and undigested meat fibers are present in pancreatitis, occult blood being found in peptic ulcer. In all cases a thorough physical examination should be made including neurologic findings, for absence of patellar reflex and Argyll Robertson pupils are cardinal signs of tabes dorsalis, which may be masked by the abdominal discomfort of a visceral crisis. The non-protein nitrogen estimation of the blood is elevated in intestinal obstruction. Due to persistent vomiting and accompanying dehydration in intestinal obstruction, there are changes in the ionic balance of the blood somewhat akin to phenomena observed in pernicious vomiting as noted in pyloric obstruction. Thus, chlorine and sodium are lost, the blood chlorides fall, and alkalosis ensues. These laboratory findings are in proportion to the height of intestinal obstruction, for low large bowel obstruction presents minimal and late laboratory findings.

Intestinal obstruction may be partial, complete, acute, or chronic. Acute obstruction is due to sudden narrowing or occlusion of the intestinal lumen. If in addition there is obstruction to the vascular supply of the bowel wall, strangulation ensues. This produces violent peristalsis, with the proximal gut vainly lashing itself in an endeavor to force the fecal current past the obstruction. Peristalsis distal to the obstruction empties the bowel to some degree and remains contracted. The initial cause is mechanical in nature and is usually actual blockage. Peristalsis above the block ceases early and the bowel becomes distended with hemorrhagic fecal fluid and gas which is poorly absorbed by the bowel wall. The gas is formed in great amount by the putrefaction of the stagnated intestinal contents, none of which can pass beyond the site of obstruction. The stagnant intestinal contents become charged with powerful toxic material the nature of which has been shown by Whipple (43) to be due to excessive breakdown of tissue protein, which causes absorption of a proteose into the blood. Experimentally, this

proteose isolated from obstructed loops of intestines, when injected into fasting dogs, produces profound symptoms of depression, followed in cases in which doses were sub-lethal by recovery in from 24 to 48 hours. Along with these symptoms, nitrogen elimination by the urine was increased 100 per cent. The inaugural shock is due to sudden production of obstruction, and at this stage the distended bowel is thinned. Later, the general depression as described is resultant of toxic absorption and at this time the bowel is congested and edematous, with bleeding occasionally from the mucous membrane, desquamation, and erosion. This permits bacterial invasion through the bowel wall into the peritoneal cavity, and sometimes actual perforation at sites of erosion. Peritonitis then is produced, with paralysis of the entire intestinal tract.

Intestinal distention in any form produces some degree of impairment of circulation in the intestinal wall. When actual strangulation occurs, it usually involves initially the venous, and then the arterial blood supply. Thus, in earlier stages of strangulation, the gut is of purplish hue, edematous and distended, with sero-sanguineous transudate in the bowel lumen and to a lesser extent in the peritoneal cavity. When arterial blockage supervenes, gangrene occurs. If there is immediate and absolute venous and arterial obstruction, gangrene is immediately produced, with slight distention of the strangulated coil, which is greenish-black in color. Peritonitis then rapidly follows and perforation is common.

Normally, small intestinal gas is never visualized roentgenographically, for the small amount of air ingested with food and the minute amount of gas produced by fermentation and bacterial action are rapidly absorbed and propelled forward by peristaltic action, which prevents any local accumulations. Inasmuch as it has been proven experimentally that retardation of the intestinal circulation is accompanied by gaseous dilatation of the bowel, it is rational to consider slow transit of intestinal con-

tents as conducive to stagnation, fermentation, and gaseous formation, which in turn produce intestinal dilatation with retardation of circulation and more gas formation. Thus, a vicious circle is established, and cause and effect cannot always be accurately determined. This theorization, however, does not adequately explain the *modus operandi* of the gaseous distention in cases of congenital atresia in newborn infants who have never taken food. Accordingly, the rôle of the sympathetic nervous system control must be seriously evaluated, for in shock and in ureteral colic with concomitant shock there is slight dilatation of the entire intestinal tract, particularly the large bowel, which is a diagnostic differential point. The findings are explicable upon the basis of retarded circulation of the splanchnic vessels resultant of shock. This probably explains the intestinal distention noted in cases of visceral crisis of tabes dorsalis.

The causes for acute intestinal obstruction can be classified as follows: I—Outside the Intestines. (a) Strangulation by bands, adhesions, and through apertures, including internal and external herniæ; (b) volvulus, which is a twisting of the loop of bowel upon its mesenteric axis; (c) paralytic ileus, which is paralysis of the muscular walls of the intestine, and may follow any abdominal shock, *viz.*, abdominal operations and injuries, peritonitis, embolus or thrombosis of the mesenteric vessels, and, rarely, pneumonia; (d) pressure of tumors is rare. II—In the Intestinal Wall. (a) Intussusception (a common cause for obstruction in children); (b) tumors and strictures; (c) idiopathic dilatation of the colon. III—Within the Lumen. (a) Impacted feces, gallstones and other foreign bodies. Any chronic obstruction may become acute, under suitable conditions. The intensity of the changes and symptoms of acute intestinal obstruction depends upon (1) the site of strangulation, being considerably more severe in the small than in the large intestine; (2) the length of bowel involved; (3) the degree of vascular occlusion which

is directly related to the tightness of strangulation.

Generalizations that are helpful are as follows: The male sex is especially prone to hernia and volvulus; the female sex, to pressure by tumors, obstruction due to gallstones and fecaliths; children, to intussusception and congenital stricture and persons beyond 50 years of age, to malignant growths.

Preliminary survey roentgenologic examination of the acute abdomen was first advocated by Schwarz (33) in 1911, in Europe, and by Case (8) in this country, in 1915. It has been most unfortunate that roentgenologic examination of the acute abdomen, even in cases in which intestinal obstruction is strongly suspected, has been sadly neglected. This has probably been due to the unfamiliarity of the referring physician with the diagnostic value of roentgen study, and in a great measure to the radiologist's lack of confidence or ability to formulate a diagnosis. Even at the risk of being dogmatic, one can state that practically every case of intestinal obstruction presents some diagnostic feature which would enable an experienced, competent radiologist to arrive at a definite diagnosis. This statement is made unqualifiedly, for the customary lapse of time from onset of symptoms until hospitalization is such that roentgen signs are invariably present. In the vast majority of cases merely a preliminary scout roentgenogram of the abdomen would suffice to establish the presence, and often the site, of the intestinal obstruction.

In the average normal individual, collections of gas are observed only in the stomach (*magenblase*), and occasionally in the duodenal bulb, commonly in the colon, and rarely in the terminal ileum, except when enemas have caused retro-pulsion of the colonic gas beyond the ileocecal valve. One can, therefore, infer a pathologic state in the presence of gas in the small intestinal tract, regardless of degree. This is the favorable time for prompt diagnosis, for one should never delay until dilatation of the proximal in-

testinal loops occurs, in so-termed "step-ladder" fashion, with manifestation of fluid levels. This too common practice will not aid in diminishing the terrific mortality rate; for, when the latter findings are present, the obstruction has been of considerable duration. The same emphasis should be placed on revision of roentgenologic criteria of intestinal obstruction as has been found imperative regarding clinical criteria. It should be a radiologic dictum that small intestinal gas of any degree, with or without associated signs of abdominal distention, is strong presumptive evidence of intestinal obstruction. Fluid levels are noted much later in intestinal obstruction, produced by the intestinal contents assuming a dependent position, with overlying gas, occurring in various segments of the intestinal tract. This phenomenon is noted only in the erect or lateral positions. The above statements apply mainly to acute small intestinal obstruction, for in chronic or subacute partial obstruction, generally no abnormal gaseous collections are noted. A portable examination, while not most satisfactory, will suffice, if the patient's condition does not warrant moving him. If feasible, however, the examinations should be made with the patient in the erect position, or at least in the recumbent posture, with an additional lateral projection. The use of the grid diaphragm is desirable but not indispensable.

In the subacute or chronic type of intestinal obstruction, it not only is permissible clinically but it is mandatory to supplement the examination with the administration of a barium meal, and study the transit of the opaque meal through the intestinal tract. The diagnosis in these cases is generally difficult and there is no immediate need for surgical intervention.

Usually, it is not difficult to distinguish between dilated small and large intestines. Characteristically, the central position of small intestinal loopings, having a herring bone appearance of the stretched valvulae conniventes, with a tendency for the loops to assume a transverse "step-ladder"

pattern, is in contrast to the dilated large intestines which present pathognomonic haustrations, and are situated in the customary colonic peripheral position. One should not err in attempting to distinguish large from small intestines by the relative size of lumina, for not infrequently small intestinal caliber will distend to a far greater degree than moderate dilatation of the colon. Since a fair percentage of adults above 40 years of age have colonic diverticulosis, observation of them will readily enable one to differentiate the colon. Fluid levels are noted earlier and are more numerous in small intestinal loopings, which fact is accounted for by increased secretion and diminished absorption of fluids from the gut proximal to the obstructive site. A similar condition exists in paralytic ileus.

A further refinement in roentgenologic diagnosis is the localization of the obstructive site, and although not always possible, should nonetheless be attempted, for accurate localization enables the surgeon to choose the proper site for incision, thereby eliminating a general abdominal exploration. It should be borne in mind that dilatation of the bowel ensues in regular orderly fashion, from the most proximal portion of the large bowel, extending distalward toward the site of obstruction. This phenomenon is best observed in obstruction in the sigmoid colon region, where the first colonic dilatation is noted in the cecum, and then progressive distention of the colon toward the sigmoid. This is an extremely important consideration and explains a rather common error in diagnosis, which occurs as follows: when dilatation of the colon has just reached the splenic flexure at the time of roentgenographic exposure, one might readily consider this the obstructive site, whereas, actually, the progressive dilatation had as yet not reached the true obstructive site in the sigmoid colon. This phenomenon does not occur in similar manner in small intestinal obstruction, for almost immediately above the site of obstruction, distention of the intestine is

noted. Relevant to large bowel obstruction, there is no reasonable excuse for committing an error as to its site, for a supplementary opaque enema examination is always indicated in such a case regardless of inferred etiology. The barium clysma affords further important information concerning the etiology of the obstruction, and in certain instances may correct the condition, *viz.*, spontaneous reduction of an intussusception is not at all uncommon during an opaque clyster examination. The accurate localization of small intestinal obstruction is more difficult, but if one remembers the average situation of the small intestinal groups, as so well described by Cole and his collaborators, the procedure will be greatly simplified. If the gas-dilated bowel is in the lower portion of the abdomen, one can assume that it is in the terminal ileum, whereas if in the upper abdomen, the obstruction is probably in the jejunum. It is a very difficult task to differentiate jejunum and ileum by their characteristic mucous membrane patterns, for while the jejunum presents more clearly outlined transverse striations produced by the valvulae conniventes, compared to the smoother appearance of the jejunum, the appearance of the plicae circulares is so distorted when distended, and normally the transition is so gradual, that this does not afford a reliable differential point. Occasionally, however, this appearance is so characteristically striking that an exact diagnosis can be readily made.

Various estimates have been made regarding the earliest time at which small intestinal gas can be visualized in cases of obstruction. In simple obstruction, the writer and others have observed gaseous collections within from four to five hours after the onset of symptoms. In colonic obstruction the elapse of time before definite distention signs are demonstrable is much longer and more variable. In strangulation obstruction, gaseous shadows are observed still later, and the minimal bowel distention tends to remain localized to the strangulated site for a considerable length of time, with no further associated

dilatation of the proximal colon. Terminally, there is evidence of generalized peritonitis. Nonetheless, the criterion that the presence of small intestinal gas is always of pathologic import holds true; and fortunately in this entity, the small intestines are the site of predilection, where it can usually be readily diagnosed. In occlusion of the mesenteric vessels, gaseous distention occurs somewhat later than in simple obstruction, and aside from clinical signs of regional tenderness and evaluation of the common sites of strangulation which are most commonly external herniae, there is no roentgenologic differentiation of the two. Lack of localized distention with rather diffuse small intestinal dilatation suggests vascular occlusion.

A question of rather vital importance arises: Can one correctly diagnose either intestinal obstruction or peritonitis roentgenologically, if an opiate such as morphine has been administered to the patient? This resolves itself into a discussion which is more theoretical than practical if one attempts to evaluate the various conflicting reports upon the action of opiates upon the small intestinal tract. To be sure, the burden of proof seems to favor the action of retardation of small intestinal activity, but even this has recently been seriously challenged. Of actual importance is the question as to whether or not the exhibition of an opiate hypodermically can produce abnormal presence of gas in the small intestines or even distention of the bowel. In the author's experience this phenomenon has never been observed or proven satisfactorily by his colleagues. In the acute abdomen we are confronted with an urgent and serious issue, which requires swift deliberation, for delay jeopardizes the patient's life in wellnigh geometrical progression. One should never delay, therefore, until the effects of an administered opiate disappear before culminating a diagnosis, for then the golden opportunity has forever passed. It is exceptional to find that an opiate has not been given prior to hospitalization, which fact (if one concurs in the belief that its effects might

simulate intestinal obstruction) would at once invalidate any conclusions drawn from an early roentgenologic examination. The incontrovertible fact remains, that the incidence of correct diagnosis by roentgenologic methods has been surprisingly high when employed with administration of an opiate. Actual experience attests to the fact that in many cases in which the diagnosis is withheld until the effects of the narcotic have worn off, and there is concomitant disappearance of signs of distention roentgenographically, one should not necessarily consider this as reliable evidence that the distention is due to the effects of the narcotic. Not infrequently, there is a recrudescence of symptoms (with establishment of pathognomonic criteria and confirmation by operation) of intestinal obstruction. This has recently been very much impressed upon the author by a short series of cases in which it occurred. The explanation of the above is simply that it is reasonable to assume that in a certain fair percentage of cases the obstruction spontaneously corrects itself, as has been observed roentgenoscopically in intussusception during an opaque enema examination. This spontaneous correction, which is probably fairly frequent in volvulus and herniæ, particularly of the Richter type, furnishes a fertile field for speculative reasoning. Further scientific study is necessary to decide incontestably as to the true nature of this sometimes confusing factor.

With a little thought given to it, the diagnosis of mechanical ileus is essentially simple. With a history of intermittent colicky pain suggestive of obstruction to some hollow abdominal viscus, and roentgenographic demonstration of small intestinal gas, one can then further differentiate between paralytic ileus and mechanical ileus, by means of abdominal auscultation. The presence of peristalsis indicates mechanical obstruction, and its absence, paralytic ileus. From the nature of the lesion, mechanical ileus should present no gas or fecal material in the distal portion of the bowel, and the rectum should

be collapsed, but such is not a reliable roentgenographic finding. Due to the lack of peristalsis in paralytic ileus, the bowel becomes distended with gas. Usually the large and small bowels are dilated and the rectum shows some degree of distention.

In the acute abdomen more than in any other radiologic problem, the consultant radiologist's diagnostic acumen, clinical ability, and judgment tempered with radiologic skill earn him an enviable position, for so frequently can he be of inestimable aid in deciding the proper therapeutic procedures. If radiologists as a group would always keep foremost in their minds the fact that they are consultants not only in the limited field of radiology as a specialty, but as regards medicine as a whole, they would not hesitate to employ all the methods of physical diagnosis in conjunction with what is merely a specialized method of physical diagnosis of internal examination, namely, roentgenology. It is incomprehensible why many radiologists will unhesitatingly inspect or palpate an abdomen, as such a method of examination is commonly performed in routine gastro-intestinal examinations, but erroneously consider percussion and auscultation, temperature and blood pressure recordings, as transgressions beyond the pale of radiology. We as radiologists are constantly confronted with a problem that the surgeon presents for diagnosis: What is causing the post-operative abdominal distress and meteorism? Is it paralytic ileus or mechanical obstruction, and, if the latter, what are its approximate site and probable cause? Are there any further untoward complications definable? These are typical problems which must and can be answered with fair decisiveness by roentgenologic study, and it is the radiologist's decision which often determines whether a secondary operation is necessary or contra-indicated. Thus, mechanical obstruction may be resultant of post-operative adhesions, and severance of the synechiæ affords prompt relief of symptoms; or again, in the

presence of paralytic ileus, further peritoneal insult may terminate fatally. One must not forget, however, that in the late stage of obstructive ileus there is transitional terminal adynamic ileus, attributable in the main to superimposed peritonitis.

It has long been rumored that the administration of barium by mouth, in the presence of intestinal obstruction (particularly of the acute type), is a dangerous procedure and contra-indicated. This opinion is apparently based upon the assumption that perforation of the bowel is an omnipresent danger, and there is the additional possibility of transforming an incomplete into a complete obstruction by barium impaction. There is such a notable lack of evidence as to the former that it can almost be dismissed, but it must be stated in fairness that it is remotely possible that such might occur if a barium meal were given when an unrecognized perforated peptic ulcer were present. The mortality has been no higher in consequence thereof, for diagnosis is always immediately established and an emergency operation performed. Conceding the point, for the sake of argument, that barium impaction does occur in a small proportion of cases, what dangerous cataclysm has been precipitated? Since obstruction exists it should be rectified, and if total obstruction is produced, then immediate surgical intervention is all the more indicated, and unmistakable clinical and roentgen findings are then manifest. Furthermore, barium ingestion should never be undertaken until a preliminary scout roentgenogram of the abdomen has been procured; and if rupture of a hollow abdominal viscus is present, it is readily noted by the presence of free gas beneath the diaphragmatic cupola. The use of umbrathor in lieu of barium sulphate will serve a similar purpose and cannot possibly cause an impaction.

In every instance in which large bowel obstruction is suspected and occasionally when terminal ileal obstruction is suspected, a supplementary opaque enema examination should be made, if feasible, to determine or verify the site and possibly

the cause of the obstruction. The terminal ileum is very frequently well visualized during a barium clyster examination by ileocecal regurgitation, and much valuable information can be obtained in this manner, regional ileitis being diagnosed, if present. It is not essential to employ the double contrast method of Fischer, for the ordinary method with an additional post-enema evacuation roentgenogram usually affords sufficient information without the added discomfort to the patient, or remotely possible perforation due to over-distention with air. In the acute abdomen this very valuable method of Fischer has inherent disadvantages which seem to outweigh its potential advantages. The best technic consists of obtaining exposures under roentgenoscopic control, placing the patient in the best position for visualization of the intestines. Particularly in the sigmoid colon region, both left and right oblique projections are necessary. Rarely has combined oral and colonic barium administration been necessary, the one procedure tending to obscure the outline of the other.

Although intestinal obstruction can be differentiated from generalized peritonitis in a fair percentage of cases, this is of more academic than practical importance, for in practically all cases operative intervention is imperative. In some degree, however, the type of therapeutic procedure varies with the issue and a definite diagnosis might be of some additional value. There are well-defined criteria which afford an exact roentgenologic diagnosis of peritonitis, but the findings obviously vary depending upon the duration, extent, and type of infection present. In an average, moderately advanced, general peritonitis there is a moderate degree of both small and large intestinal dilatation which rarely approaches that noted in intestinal obstruction. Due to serous exudative changes, a homogeneous shadow in the flanks is visible, and the normally discernible sub-peritoneal adipose tissue lines, as well as the adipose tissue spaces between the transversalis and internal and external

oblique muscles, are hazy in outline or obliterated, due to inflammation and exudation into the abdominal wall. This is noted approximately twelve hours after the onset of symptoms. Since this loss of outline is resultant of contiguous extension of infection and inflammatory edema, it follows that this sign is of value only in a positive sense, *i.e.*, when it is obliterated it gives definite evidence of peritoneal inflammation. When it is visible it is of no diagnostic significance whatsoever. Since peritonitis eventually is causative of paralytic ileus, the finding of free peritoneal fluid is inferential evidence that the primary cause was peritonitis rather than uncomplicated intestinal obstruction. Localization of fluid, especially in the appendiceal region, is readily demonstrated by trans-abdominal projections; that is, with the patient in the dorsal decubitus position, and the rays directed anteroposteriorly. If no associated effusion is evident, the coils of gut present well defined and closely approximated walls, whereas concomitant exudation produces an impression upon the coils by pushing between the intestines. Added evidence of plastic exudative changes in peritonitis is the presence of dense bands between the dilated loops of gut, with associated thickening of the bowel wall and haustra in the colon. An underexposed roentgenogram is sometimes useful in soft tissue differentiation and will well demonstrate a generalized haziness of outline of the viscera, with increased diffuse density.

Partial intestinal obstruction presents no gas-dilated intestinal loops unless intermittently complete obstruction occurs. One may examine the patient at various times and totally different findings may be present; thus, during the partial obstructive stage, the sole roentgen finding may be retardation of transit of the barium meal through the affected region of bowel, whereas typical total obstructive signs may be demonstrated when precipitated. This makes serial examinations of one-hour intervals necessary. Attention must be directed to detection of malformed small

intestinal loops, for this might well be the diagnostic feature, as is noted in effects from adhesions, tuberculous peritonitis, incarceration of internal herniæ, and regional ileitis. A diagnosis of functional spastic ileus should be cautiously made, for this is extremely rare and often the true nature of the lesion is proven to be of organic nature.

A rather common syndrome is the presence of small intestinal distention, rather limited to the left abdomen, which, in the absence of prior surgical operation to suggest possible adhesions, is very likely to be appendicular disease or abscess causing the obstruction. An additional opaque enema examination presents further diagnostic features if appendiceal abscess is present. There is some displacement of the terminal ileum medially with narrowing of its lumen, deformity of the caput ceci and hypermotility of the cecum, irritability as shown by a tendency to shake off its contents, and lack of fixation of the cecum. A word of caution may not go amiss: an exact pathologic diagnosis cannot always be made and should not be demanded by the referring physician. Furthermore, such exact diagnosis is not always essential, the vital question being the decisive answer as to whether or not immediate operative intervention is indicated. Fecaliths and large biliary calculi have been noted roentgenographically as causes for intestinal obstruction, the latter having entered the bowel through a cholecysto-enteral fistula. The site of obstruction is commonly at the ileocecal valve. Other foreign bodies have been reported in the literature, but are so rare as etiologic factors of obstruction that they are merely mentioned for the sake of completeness; *viz.*, ascariasis, metallic foreign bodies in the mentally deranged, coalescence of grasshoppers which are eaten in the Belgian Congo, etc.

Occasionally a gall-bladder shadow can be visualized with or without calculi; but even when not discernible it aids in the sense of negativity. Cholecystography, even when employing the intravenous

method, is rarely indicated on account of the urgency of the symptoms in acute cholecystitis and gangrene, or empyema of the gall bladder. Curiously, when such has been performed very frequently the functional test approaches normalcy, in spite of marked involvement of the gall-bladder walls.

Colonic obstruction may be due to sudden occlusion of an insidiously encroaching pericolic infection, commonly secondary to diverticulitis, in the nature of frank abscess or granulation tissue formation. The surgeon is often unable to distinguish macroscopically between an inflammatory and a malignant lesion, for not infrequently neoplastic tissue becomes secondarily infected to complicate matters. Fortunately, this differentiation can be made in the vast majority of cases by roentgenologic study, for in the presence of colonic diverticulosis, with no loss of the relief pattern of the mucous membrane at the suspicious site of narrowing or obstruction, and with associated regional tenderness, a diagnosis of benignity is justifiable and usually correct; however, exploration is nonetheless indicated. In the author's experience, complete obstruction rather than gaping canalization permitting passage of fluids is strongly suggestive of a benign lesion. Rarely, a ruptured diverticulum can be demonstrated by the opaque enema, as a small barium-filled fistulous tract through the colonic wall or into the pericolic structure. This walled-off inflammatory tissue is most commonly found in the sigmoid colon.

Excretory urography is indicated in suspected ruptured kidney or bladder, for extravasation of the dye-laden urine into the perirenal structures or through the vesical wall can be well demonstrated. Incidentally, the same roentgenogram may demonstrate concomitant fractures of ribs, spine, or pelvis. Definite roentgen signs of acute calculous obstruction of the ureter are noted, with or without visualization of the urinary calculus, for an increased density of the renal shadow associated with delay in excretory function of the involved

side is strongly suggestive and almost pathognomonic of this condition.

Perforation of a hollow abdominal viscus is readily diagnosed by the finding of free peritoneal gas beneath the diaphragmatic cupola. If this possibility is questioned post-operatively, one must not lose sight of the fact that from 24 to 48 hours are required for absorption of the air included in the peritoneal cavity when a laparotomy has been performed. Fluid levels are usually late findings and indicative of sub-diaphragmatic abscess formation, for very generally gravitation of gastric chyme and gas does not occur in sufficient amount to present this phenomenon when a peptic ulcer ruptures. A hepatic abscess can be differentiated by its position in the anterior and lateral projections within the hepatic tissue. Fixation and elevation of the right diaphragm are fairly early findings in sub-diaphragmatic abscess formation. Fluid in the lesser omental bursa can be demonstrated by displacement signs with administration of a barium meal, which is generally associated with a penetrating ulcer in the contiguous region; *viz.*, the posterior wall of the stomach. Caution must be taken not to cause undue pressure upon palpation of the penetrating ulcer which might result in a further rupture.

A supplementary examination of the chest, even if only roentgenoscopy, cannot be too strongly emphasized, in any atypical form of suspected abdominal catastrophe, for lobar pneumonia and diaphragmatic pleuritis can closely simulate appendicitis. This is more common in children, in whom physical signs are more difficult to elicit; but fortunately, pneumonic infiltration or restriction and elevation of diaphragm in pleuritis is amenable to roentgenologic demonstration very early.

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CLEIDOCRANIAL DYSOSTOSIS (MUTATIONAL DYSOSTOSIS)

WITH A CASE REPORT

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CLEIDOCRANIAL dysostosis is a condition wherein single or multiple abnormalities of osseous development occur spontaneously or from inheritance. It is so named because all the patients in whom it has been found have had defects of the clavicles and most of them have had skull deformities. An excellent review of the condition up to 1929 was given by Fitchet (1). Other references are listed in the bibliography.

The following abnormal conditions have been reported:

Skull and Head.—In cases with skull and bone defects, radiographs of the skull may show large areas not ossified, failure of fusion at the fontanelles and sutures, and the presence of multiple wormian bones. The patency of the fontanelles may be permanent. Metopic sutures are common. Failure of ossification along the sagittal suture may occur. There may be openings at the bregma and asterion. One defect of the right orbital ridge has been reported. The occipital foramen may be tilted forward and be higher than normal because of deformed sphenoidal and facial bones. The bones of the base of the skull and face are small with small nasal accessory sinuses. The jaws are often prognathous. There may be an absence of the nasal and lachrymal bones. The deciduous teeth persist longer than normal—up to 12 years—and there is delayed eruption of the permanent teeth which may have faulty implantation and enamel defects. There may be an absence of some of the permanent teeth, particularly the canines, or development of supernumerary teeth.

Shoulder Girdle.—Defective formation of one or both clavicles is the most common finding from roentgen examinations. In a

few cases the clavicular defects are the only abnormalities found. A variety of changes in the clavicles, from a simple transverse defect of the middle third, sometimes mistaken for an ununited fracture, to complete absence of both clavicles, have been reported. In the majority of cases the defects are found at the sternal ends, but examples in which the acromial ends have been missing have been illustrated. A thin fibrous section, from a failure of union of the medial and outer halves, may exist in the shaft. In these cases the opposing ends are rounded and generally overlap. The acromial processes may show abnormalities with absence of the articular surfaces at the acromioclavicular joints. Absence of the supraspinous fossa of the scapula may occur, in which case the root of the spine forms the upper border of the scapula.

Arms and Forearms.—Partial or complete absence of the radius has been reported. The styloid processes of the radius and the ulna may be at the same level, whereas normally the radius is longer.

Hands.—Roentgenograms of the hands show multiple deformities which are characteristic of the condition. The distal phalanges are without their ungual expansions; they are short and conical in shape. The middle phalanges are much shorter than normal and their lateral borders are concave, almost resulting in a dumb-bell shape. The proximal phalanges are expanded in their proximal halves, and there is some narrowing of the shafts with increased density of the middle and distal thirds. The metacarpal bones are expanded at their extremities and narrowed in the middle thirds, with some increase in

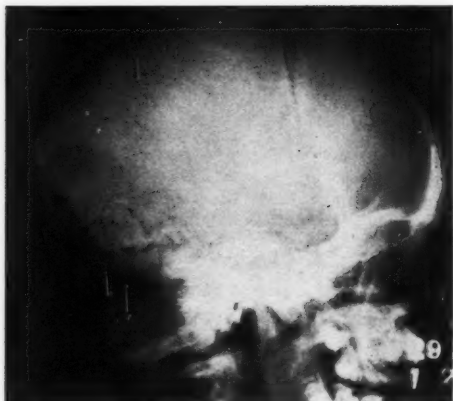


Fig. 1. Roentgenogram of the lateral skull. Note anterior fontanelle, wormian bones, sella turcica, absence of mastoid, dental development, and small maxilla.



Fig. 2. Roentgenogram, showing the postero-anterior view of the skull. Note the anterior fontanelle, wormian bones, dental development, and small facial bones.

the compact tissue at this level. Epiphyses frequently are seen at both ends of the basal phalanges and metacarpal bones. One case of elongation of the second metacarpal bone has been reported.

Spine.—Several abnormalities in the development of the spine have been reported. Kyphosis, lordosis, and scoliosis may occur. Spina bifida has existed. Cervical ribs are common. One patient with an extreme scoliosis showed bifid bodies of the seventh to eleventh thoracic vertebræ and defective laminae in the fourth and fifth lumbar and all the sacral segments.

Pelvis.—The pelvic bones frequently are abnormal in development. Before puberty the pelvic canal is narrowed and the joint spaces are considerably widened, including the spaces between the ischium, ilium, and pubis at each acetabulum. After puberty the pelvic joint spaces are narrowed and irregular in outline, the mature pelvis having the broad, squat appearance associated with malformed, defective joints. The pubic bone may be missing. In two sisters with cleidocranial dysostosis, there were defective laminae of the first sacral segment.

Thighs and Legs.—Disorganization of ossification of the neck of the femur which may result in coxa vara occasionally is

found. Genu valgum is noted in many cases. Partial or complete fibular absence has been reported. In general, the long bones of the arms, forearms, thighs, and legs, as well as the ribs, are least affected.

Feet.—The phalanges and metatarsal bones of the feet show the same typical changes as the phalanges and metacarpal bones of the hands. One case each of a double metatarsal bone and a supernumerary toe have been reported. Poor development of the astragalus and calcaneus is frequent. The astragalar neck is very thin, and the calcaneus is shortened.

Clinical Observations.—The skull usually is brachycephalic, with an increase in the lateral diameter. The frontal, parietal, and occipital bosses often are unusually prominent. The patent sutures and fontanelles are palpable, and depressions can be felt after these unite. The bridge of the nose may be sunken. The palate may be high or cleft. The prognathism of the jaw and the faulty dentition are prominent findings.

If defects in the clavicles occur, there is an unusual mobility of the shoulders.

When the clavicles are completely missing, the shoulders can touch each other anteriorly, as in the case illustrated by Pills-

ever, there is mental deficiency or a definite psychosis. A few defects of the soft tissues have been reported. One case each of

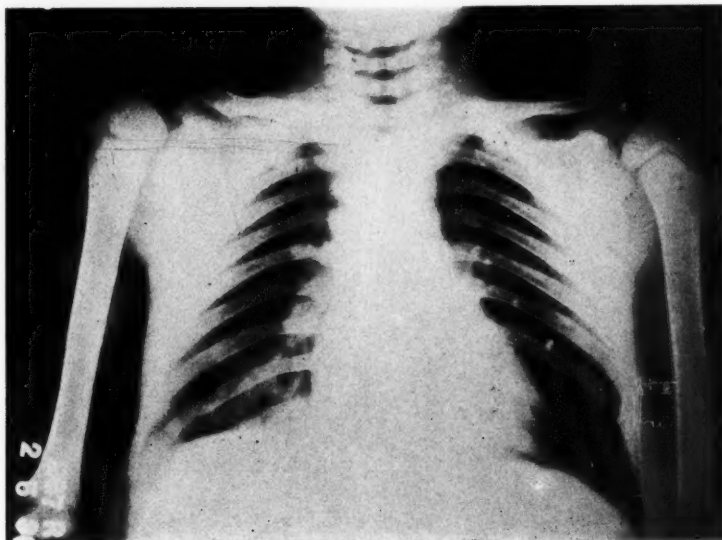


Fig. 3. Roentgenogram of the shoulders. Note normal clavicles, acromial defects, absence of coracoid processes, and failure of union in the cervical vertebrae.

bury (2). In one patient there was pressure of the outer fragment of the clavicle upon the branchial plexus, with pain which was relieved by removal of the fragment. No pain usually results from the dysostoses.

As noted above, although a straight spine is the rule, there may be gross visible deformities.

Deformities of the feet described as talipes cavus and calcaneocavus, resulting from posterior displacement of the line of weight-bearing, have been described.

The basal metabolic rate is variously reported as normal, minus 15 per cent, and plus 37 per cent.

In all reported cases, blood calcium and phosphorus concentrations have been found to be normal.

As a rule, patients with cleidocranial dysostoses suffer no pain nor disability from the osseous defects. The mental ability usually is good, and the stature is not necessarily decreased. Often the condition is unsuspected. Occasionally, how-

ever, there is mental deficiency or a definite psychosis. A few defects of the soft tissues have been reported. One case each of

inguinal hernia and prolapse of the uterus in a virgin have been found. Muscular deformities have been described.

About the only condition that can be confused with cleidocranial dysostosis is delayed rickets. In the latter condition prominent cranial bosses, delayed closure of the sutures and fontanelles, and poor dentition are present. However, the changes in the clavicles, metacarpal, and metatarsal bones which occur in dysostosis are not present.

The cause of cleidocranial dysostosis seems to be mutational. The mutation appears spontaneously, and the characters may be transmitted to the second and third generations. Many family histories have been compiled showing the hereditary transmission. The characters are not dominant and are lost in two or three generations by cross-breeding. Although most observers have stressed the deformities of the clavicles, the mutation may cause changes in any bone of the body.

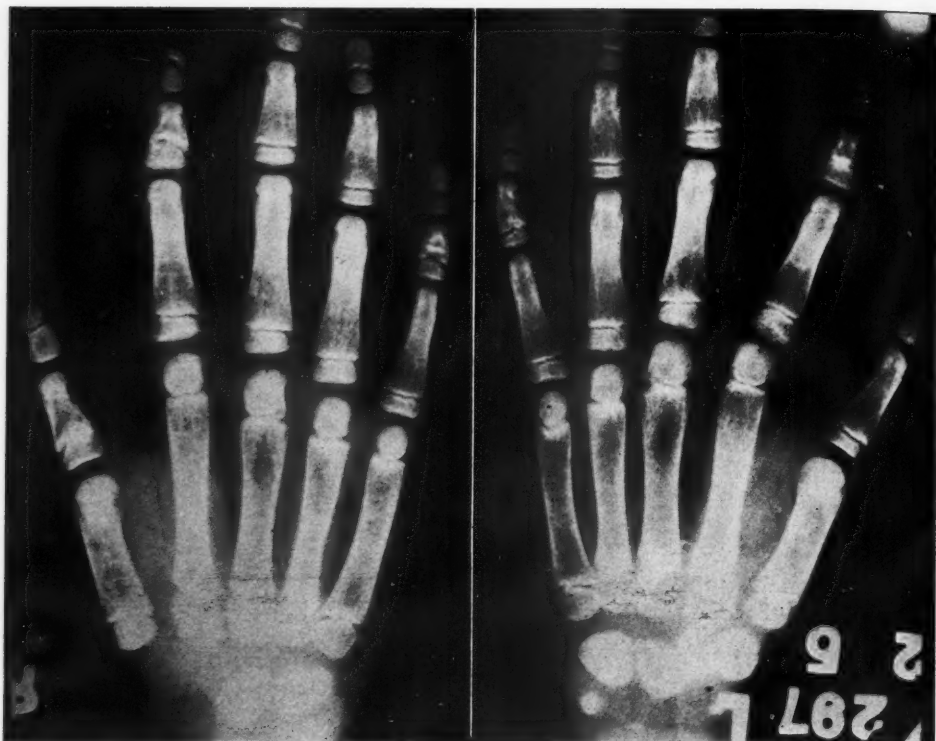


Fig. 4. Roentgenogram of the hands. Note carpal development, double metacarpal epiphyses, and abortive epiphyses at the distal ends of the phalanges.

The following case report of cleidocranial dysostosis in a ten-year-old boy is presented because:

- (1) The condition is rare but liable to be encountered at any time;
- (2) This patient has nearly all of the lesions described in the literature;
- (3) Studies have been made from the clinical laboratory viewpoint to determine, if possible, whether abnormal hematologic conditions, etc., exist;
- (4) The clavicles apparently are normal, indicating that possibly the defects of these bones have been overstressed.

The patient, W. E., is a white boy, aged 10 years, of Nordic parents. On Jan. 10, 1936, because of a complaint of headaches, he was brought to the Isaac Folsom Clinic, University of Arkansas School of Medicine, by a school nurse. At the Clinic he received a thorough physical examination in

the Department of General Medicine, and was referred to the Department of Pediatrics where he was further examined by Dr. I. J. Spitzberg. Then he was sent to the Department of Roentgenology, with a tentative diagnosis of rickets, congenital syphilis, or congenital dislocation of the right hip, for roentgenographic examinations of the pelvis, right hip joint, and skull. Because the roentgen findings indicated a diagnosis of congenital dysostoses, the entire skeleton and lungs were roentgenographed. At the same time an exhaustive laboratory examination was conducted. Unfortunately, because of the onset of fever from an acute bronchitis which has not subsided, the basal metabolic rate could not be determined.

Family History.—Nothing is known of either the paternal or maternal great grandparents. The paternal grandfather died



Fig. 5. Roentgenogram of the pelvis and hips. Note absence of right pubis, defective left pubis, coxa vara of the right hip, and poor union of the sacral segments.

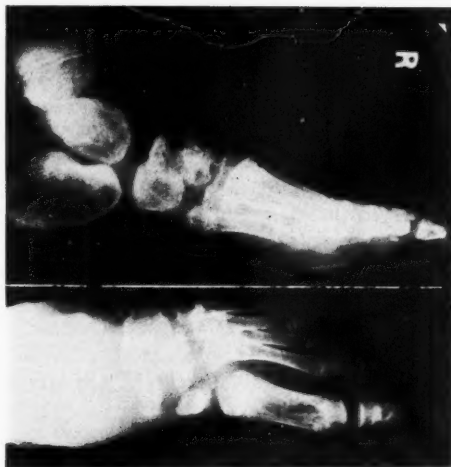


Fig. 6. Roentgenogram of the foot. Note retarded tarsal development and double metatarsal epiphyses.

at the age of 48 from a paralysis of the tongue and throat muscles. The maternal grandfather died at the age of 40 from a respiratory infection. This man was said to have had a bone disease and a short leg resulting from an operation. The paternal grandmother, aged 52 years, and the maternal grandmother, aged 48 years, are living and apparently are in good health. The patient's parents are living and are considered healthy. Neither parent has evidence of clavicular, cranial, or dental deformities. The mother is 27 years of age; the father is 32. The father's occupation has been farming. The mother has had two miscarriages and has borne five living children, three of whom are healthy. A sister of the patient, aged nine years, has a partial spastic paralysis and is an idiot. From a roentgenographic examination, her bony development is shown to be normal. The family income always has been very small.

Past History.—This was obtained from the records of the Isaac Folsom Clinic and records that W. E. was born at full term and weighed eight pounds at birth. The delivery was normal. He was bottle-fed from birth. The first tooth appeared in six months. He talked at 13 months, but did not walk for 18 months. Past illnesses

have been rubeola, mumps, varicella, pneumonia, and malaria. There have been no other serious illnesses, accidents, nor operations. Although in school he has not progressed past the second grade, the boy seems to be mentally alert. There have been inadequate opportunities for school attendance. His school grades are below the average.

Present Illness.—Except that she is aware of the limp and the poor dental development, the mother has not realized that the patient is deformed. She knew nothing of the headaches which caused the chief complaint. During the last two years, W. E. occasionally has complained of pains in the knees, the attacks lasting from an hour to a day or so. His strength seems to be less than normal. There is no history of night cries.

Physical Examination.—The patient is a white child, appearing to be approximately eight years of age. His temperature is 98.6° Fahrenheit; pulse, 90; respiration, 22; height, 46 inches, and weight, 50 pounds. He walks with a decided limp of the right inferior extremity. There is a skin eruption over the lower back, buttocks, and the posterior aspect of the thighs which was diagnosed as scabies. The mucous membranes are normal in

appearance. The skull is box-like in shape with prominent frontal and parietal bosses. The transverse diameter is increased and the supero-inferior diameter is diminished. Depressions along the sutures can be palpated. The anterior fontanelle is very large, not bulging, but firm to pressure. The fontanelle extends anteriorly to a point midway between the parietal and nasal bones. A metopic suture can be felt. The eyes are negative except for photophobia. The mastoid processes are missing. The facial bones are small. The mandible is small. The teeth are irregular, carious, and dirty; the cutting edges are smooth. The neck, shoulders, thorax, lungs, heart, abdomen, spine, pelvis, genitalia, and upper extremities are negative to physical examination. The right thigh is about one and one-half inches shorter and smaller in circumference than the left. Abduction of the right thigh is limited, and adduction is increased over normal. The reflexes are normal. The right foot shows a second degree pes planus and is rotated laterally 30 to 45 degrees.

It will be noted from this examination that there is no clinical evidence of deformities of the clavicles or pubic bones. Although the roentgen films show defective development, definite pubic structures can be felt.

Laboratory Findings (by Dr. A. F. Pirniquet).—The erythrocyte count was 3,600,000 per cubic centimeter. The hemoglobin (Sahli) was 75 per cent, and the color index was 1.04. There were no erythroblasts, normoblasts, microcytes, macrocytes, megaloblasts, polychromatophilia, central pallor, nor poikilocytosis. There was no sign of erythropoieses. Slight anisocytosis was present. Basophilic degeneration was absent. The white cells numbered 10,300 per cubic centimeter and were differentiated as follows (Schilling): Myelocytes, none; juveniles, 0.5; staff cells, 8.5; adult neutrophils, 26; total neutrophils, 35; eosinophiles, 3; basophiles, none; lymphocytes, 56.5; monocytes, 5, and plasma cells, 0.5. The Arneth modification showed: basophiles,

none; eosinophiles with one segment, 0.5; eosinophiles with two segments, 2.5; myelocytes, none; juveniles, 1.5; staff cells, 8.5; neutrophils with two segments, 17.5; neutrophils with three segments, 8.5; large lymphocytes, 39; small lymphocytes, 17.5; plasma cells, 0.5; monocytes with one lobule, 1; and monocytes with two lobules, 4.

Résumé.—Double segmented neutrophils greater than triple (normally the reverse is true), and a greater number of large lymphocytes than small. There was a complete absence of blood platelets. The fragility test showed a hemolysis beginning at 0.46 per cent sodium chloride solution and almost complete at 0.28 per cent. The blood sedimentation index (Cutler method) was 20.5 in 60 minutes with a vertical curve. The blood Wassermann was negative. A blood calcium determination gave 12 milligrams per hundred mils.

Examination of the urine was essentially negative. The specific gravity was 1.012. Bence-Jones protein was absent. Considerable mucus was present.

*Roentgen Examinations.*¹—Roentgenograms were made of this patient's entire skeleton.

Head.—The parietal and occipital bones are thickened to more than twice the normal. The lambdoid, sagittal, and squamous sutures contain a large number of wormian bones. A metopic suture is present. The anterior fontanelle is large and the frontal bones are thinned on both sides. The sella turcica is divided by a nodule on the dorsal surface of the body of the sphenoid into shallow anterior and posterior fossæ. (A sella of the same type is present in a five-weeks-old colored baby who has melorheostosis in both inferior extremities.) The mandible is unusually small. Of the permanent teeth, only the first molars and the lower central incisors are erupted. The mastoids are not developed. All the facial bones are small, and no shadows of nasal accessory sinuses can be seen.

¹The films were taken by Miss Ila Wright, R.N., technician.

Spine.—Many of the dorsal arches of the vertebrae are not united. Normally these arches unite in from one to seven years. The costal elements of the lateral masses of the sacrum are not united to the bodies. All the vertebral bodies are granular in appearance. In some of them the structure appears to be cystic. The spine is straight and has the normal thoracic and lumbar curves.

Shoulders.—Both clavicles are normal in length, and there are no transverse defects. Although they normally appear at the age of two, the coracoid processes cannot be seen on the films. The left acromion shows a transverse defect near its base. The right acromion has five small fragments at its tip. These are not epiphyses, for the acromial epiphyses do not appear until the age of 15. The glenoid processes and the epiphyses of the upper ends of the humeri show roughened outlines.

Pelvis and Hips.—There is no shadow of the right pubis. The left pubis shows a transverse defect through the superior ramus but no ossification of the body nor the inferior ramus. Normally the pubic bones are ossified at an early age. The acetabuli are retarded in development. The left one seems to be developed to an extent usually present in children of seven to eight years of age; the right shows the pubic element to be missing. The right femur shows a coxa vara. The head of the right femur is considerably smaller than the left.

Hands.—The development of the carpal bones is about equal to that in a normal child of four years of age. The metacarpal bones have epiphyses at both ends. The first and second phalanges show abortive epiphyses at the distal ends. The diaphyses of the middle phalanges of the right first, second, and fifth digits are broadened and cystic or contain enchondromas. The same condition is present in the middle phalanges of the left second and fifth digits.

Lower Extremities.—The mid-portions of the femoral and tibial shafts are unusually narrow in proportion to the ends and

whether this be due to thinning of the shafts or broadening of the ends cannot be determined. Although faint growth lines are present, there is neither curvature nor periosteal change of any of the long bones. The knees, including the patellae, resemble those of a child of seven. The superior tibial epiphyses are flattened anteriorly.

Feet.—Except that in this patient the outlines are very irregular, the development of the tarsus is approximately that of a child of three and one-half years of age. The calcanei are shortened. The astragali are shortened and egg-shaped with the smaller ends posteriorly. The metatarsal bones, like the metacarpal bones, have epiphyses at both ends. The second phalanges of the great toes are either polycystic or contain enchondromas.

(The normal development of bones was ascertained from a chart prepared by Camp and Cilley of the Mayo Clinic, and from Cohn, *Annals of Roentgenology*, Vol. 4, Paul B. Hoeber, Inc., New York, 1924.)

SUMMARY

Roentgenograms of this patient's skeletal structures show nearly all of the reported dysostoses except changes in the clavicles. In addition, deformity of the sella turcica is present. The clinical laboratory findings disclose a number of blood dyscrasias, including low erythrocyte count, unbalanced white cell ratio, and an absence of blood platelets. The blood calcium is slightly elevated.

DISCUSSION

This is a case of multiple congenital dysostoses which apparently is spontaneous since there is no definite evidence of inheritance. Therefore we may consider it to be a result of mutation. The older theory that cleidocranial dysostosis is caused by amniotic adhesions was proposed before the mutational theory of evolution was formulated. However, at no time could it be said that intra-uterine or postnatal conditions could be the cause of double metacarpal epiphyses or transmission to

offspring. Fitchet's summary gives a number of family histories showing the hereditary transmission.

The case reported in this article undoubtedly falls into the classification of cleidocranial dysostosis, but differs from the standard description and the interpretation of the name because of the absence of defects of the clavicles. In the past there has been some dissatisfaction with the name "cleidocranial dysostoses." That term certainly does not fit in the present instance. Yet the condition is the same as if W. E. had no clavicles. Formerly the differential diagnosis depended upon the condition of the clavicles; therefore, it seems that a more comprehensive designation to include all dysostoses of mutational origin should be evolved. Zoölogists refer to mutations as such and append descriptive adjectives and nouns, such as "a mutational white eye" or "a mutational short wing." Such a plan would be adaptable to mutational

dysostoses in human beings and would be more logical than the inference that the clavicles *must* be deformed. Therefore, it is suggested that the diagnosis be changed from "cleidocranial dysostosis" to *mutational dysostosis*. Such a name can be modified to suit conditions, *i.e.*, "simple mutational dysostosis of the clavicles" or "multiple mutational dysostoses," etc. The proposed name would include any and all osseous changes that might be discovered.

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RADIATION FROM AN OIL-IMMERSED THERAPY TUBE

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THE intensity of the radiation from a therapy tube immersed in a large tank of oil was found to decrease as the size of the diaphragm opening in the filter holder was decreased. The smallest diaphragm used was large enough to allow all the direct radiation from the target to reach the ionization chamber. Because this decrease in intensity seemed too great to be ascribed only to the absorption of radiation originating from parts of the tube other than the target, it seemed that an ex-

cate that part of the decrease in intensity caused by the use of small diaphragms was due to the absorption of radiation which had been scattered by the oil; also, the quality of the radiation became harder as the size of the diaphragm was reduced.

APPARATUS

The high voltage rectifier was a two-valve, voltage-doubling system with condensers, designed to deliver 15 milliamperes at 200 kv. (constant) potential. It

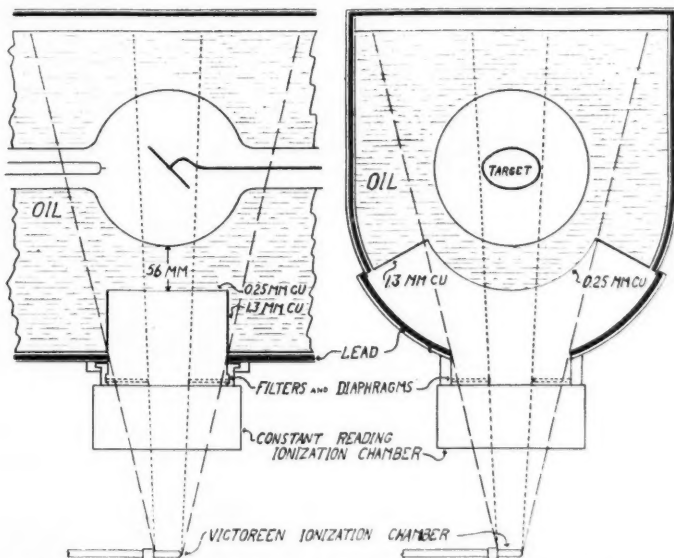


Fig. 1. Cross-sectional diagrams of tube tank. The broken lines indicate the region from which scattered radiation can reach the ionization chamber when no diaphragm is used, and the dotted lines indicate the region from which scattered radiation can reach the ionization chamber when the 2 × 2 inch diaphragm is used.

planation might be that some of the radiation which passed through the larger diaphragms was scattered by the oil surrounding the tube. A diaphragm with a smaller opening would absorb part of the scattered radiation and thereby reduce the intensity of the radiation reaching the ionization chamber. The results reported here indi-

cated that part of the decrease in intensity caused by the use of small diaphragms was due to the absorption of radiation which had been scattered by the oil; also, the quality of the radiation became harder as the size of the diaphragm was reduced.

The power supply, from a 220 volt, 50 cycle line, was very unsteady. All ionization measurements reported here were

made during a two-hour period in the mornings, during which time the line voltage seldom fluctuated more than 5 volts during a five-minute interval. At the end of the first hour of this period, a change of generators was made at the power plant. Ionization measurements made during the second hour averaged from 1 to 2 per cent higher than similar measurements made during the first hour. This increase in radiation quantity was probably due to a higher frequency and a more steady line voltage.

The x-ray tube was immersed in oil in a lead-lined tank (Fig. 1). An inverted trough below the tube reduced the amount of oil acting as a filter to a minimum thickness of 56 millimeters. A movable lead shield, with a 6×6 inch opening, over the bottom of the trough served to define the limits of the beam of radiation emerging from the tank, and allowed the angle at which the beam left the tank to be varied through an arc of 80° . The top of this trough was made of copper 0.25 mm. thick, and the sides of copper 1.3 mm. thick. Immediately below the opening in the movable lead shield was a space for diaphragms and filters. A constant reading ionization chamber, containing 2 mm. of aluminium, was mounted to the movable shield just below the space for additional filters. The oil in the tank was pumped through a radiator for cooling, its temperature gradually rising to between 55 and 60° C. when the tube was in continual operation for two hours or more.

The diaphragms were made from lead 4 mm. thick, one set having square holes cut out from their centers. The length of the sides of these holes in the different diaphragms was 2, 3, 4, and 5 inches. The smallest of these diaphragms, with a 2×2 inch hole, allowed all of the direct radiation from the target of the tube to reach the ionization chamber, but shielded the ionization chamber from most of the radiation scattered by the oil (Fig. 1).

A second type of diaphragm (lead-centered diaphragm) consisted of a piece of lead 2×2 inches square attached to the

center of a piece of thin cardboard which fitted into the filter holder. This diaphragm shielded the ionization chamber from all of the direct radiation from the target of the tube but allowed radiation scattered by the oil to reach the ionization chamber.

A third type of diaphragm was made of lead with a slot 2 inches wide cut out from the middle of one side and extending in 2 inches from the edge. This diaphragm shielded the ionization chamber from all of the direct radiation from the target and allowed the radiation scattered from only one side of the tube to reach the ionization chamber. This diaphragm could be inserted with the slot on any one of the four sides of the filter holder, so that the radiation scattered by the oil on either side or on either end of the tube could be measured.

All intensity measurements were made with a Fricke-Glasser X-ray Dosimeter. The data for the isodose curves were obtained from a rice phantom; the method of obtaining data for these curves has been described in a previous paper (2).

When the small diaphragms were used the position of the ionization chamber was checked with a fluorescent screen to make sure that the chamber was in the center of the beam of radiation.

RESULTS

Because of the unsteady power supply, there was considerable variation in the intensity of the radiation emitted from the tube. This made it necessary to repeat all measurements several times. In the daily two-hour period during which measurements were made it was possible to obtain one series of readings; in each series one factor, such as filter thickness, was varied. The order in which filters were used or other conditions were varied was reversed on each successive day in order that data would be obtained for all conditions both before and after the change in power supply, which occurred at the end of the first hour. The results obtained from two sets of ten such series differed from each other by less than 2 per cent. Most of the results

reported here are the average of twenty or more such series and none is based on less than ten series.

per cent for a filter of 2.0 mm. Cu. This decrease in the ratio as the filter is increased indicates that the radiation re-

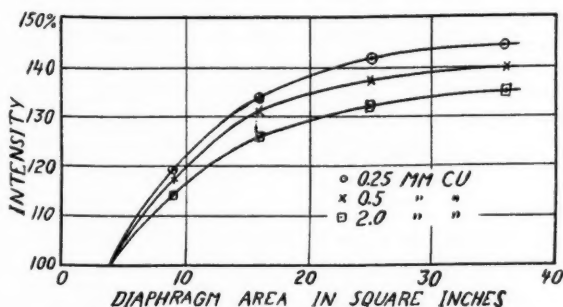


Fig. 2. Curves showing the variation in intensity of the radiation with area of the diaphragm. The intensity of the radiation for the 2×2 inch diaphragm (4 square inches) is taken as 100 per cent.

Because there was a slight increase in the output of radiation during the first five minutes the tube was in operation, no readings were taken until the tube had been in operation for at least ten minutes.

Two different x-ray tubes were in use during the period of time in which the data were obtained. The first tube, which had been in use about 1,400 hours when these measurements were begun and which had a badly warped target, had an output of radiation of 2.5 per cent less than the second tube. The quality of the radiation from the two tubes was not measurably different.

Effect of Size of Diaphragm.—The percentage variation in the intensity of radiation with change of area of diaphragm opening is shown in Figure 2. The three curves represent the variation with different filters. The measurements were made with the ionization chamber 50 cm. from the target of the tube. For all filtrations used, the intensity of the radiation passing through the 6×6 inch diaphragm (36 square inches) was much greater than that passing through the 2×2 inch diaphragm (4 square inches). The ratio of the intensity for the two diaphragms decreases as the filtration increases, decreasing from 145 per cent for a filter of 0.25 mm. Cu¹ to 135

per cent for a filter of 2.0 mm. Cu. This decrease in the ratio as the filter is increased indicates that the radiation re-

moved from the beam by the small diaphragm is of softer quality (longer wave lengths) than the direct radiation which passes through the small diaphragm, since the rate of absorption of radiation by a filter decreases as the wave length decreases. If the radiation absorbed by the small diaphragm has been scattered by the oil, it should be of longer wave length than the direct radiation, because, according to the Compton Effect, the wave length of radiation is increased by scattering.

When the 2×2 inch lead-centered diaphragm was used, the intensity of the radiation measured was equal, within the experimental error, to the difference in intensity measured with the 2×2 inch and the 6×6 inch diaphragms. When the lead-centered diaphragm was used, the only radiation which reached the ionization chamber was that scattered by the oil and that coming from the stem of the target; this was verified by pin-hole pictures taken with the pin-hole placed at the ends of the ionization chamber.

The difference in the intensity and quality of the direct radiation (2×2 inch diaphragm), the scattered radiation (lead-centered diaphragm), and the combination of aluminium (2 mm.) in the constant reading ionization chamber are omitted for the sake of brevity. The stated value of the copper filter always includes the 0.25 mm. of copper which forms the top of the inverted trough in the tube tank.

¹ In stating the values of filters, the constant thickness of oil in the tube tank and the constant thickness

of the two (6×6 inch diaphragm) is shown in Table I, for a filter of 0.5 mm. Cu. The quality of the total radiation, as shown by the effective wave length and the half value layer, is harder than that of the scattered radiation and softer than that of the direct radiation. This indicates that the radiation absorbed by the small diaphragm may have been scattered by the oil and thereby become softer in quality.

An increase in the distance between the ionization chamber and the target of the tube would produce a change in the volume of oil which could scatter radiation to the ionization chamber, and might produce a different ratio between the intensities of radiation measured with diaphragms of different sizes. Measurements made at 70 cm. distance gave results which differed from those made at 50 cm. by less than the experimental error in the measurements. With greater differences in the distances there might be a measurable difference in the ratio.

Origin of Scattered Radiation.—In order to determine the distribution around the tube of the source of the oil-scattered radiation, the diaphragm with the opening in the side was used, thereby making it possible to measure only the radiation scattered by the oil in front of, from the sides of, or behind the tube. The intensity of the radiation scattered from in front of the tube (the cathode end) was found to be 90 per cent of that scattered from either side

of the tube, and the intensity of the radiation scattered from behind the tube (the anode end) plus the stem radiation was 55 per cent of that scattered from either side or 60 per cent of that scattered from in front of the tube. If this radiation is largely scattered by the oil, these are the results that in general would be expected from the known distribution of the intensity of the radiation around a tube. In addition to the variation in intensity of the radiation in different directions from the tube, the intensity of the scattered radiation from the different sides of the tube would be affected by the difference in distribution of the oil around the tube. That the decrease in intensity of the radiation caused by using small diaphragms is not entirely due to the absorption of stem radiation by the diaphragm is shown by the fact that the intensity of the radiation from behind the tube, which included the stem radiation, was less than that from either side or from in front of the tube.

Copper Absorption Curves.—Copper absorption curves for the total radiation (6×6 inch diaphragm) and the direct radiation (2×2 inch diaphragm) were made and compared with the standard absorption curves published by Taylor and Singer (1). By shifting the co-ordinates to allow for a difference in initial filtration, the absorption curves for both the total and direct radiations were found to coincide very well with the 180 kv. (constant) standard

TABLE I.—COMPARISON OF DIRECT, SCATTERED, AND TOTAL RADIATION; 180 KV., 8 MILLIAMPERES, 50 CM. DISTANCE, FILTER OF 56 MM. OIL + 0.5 MM. CU + 2 MM. AL

	Direct Radiation (2×2 Inch Diaphragm)	Scattered Radiation (2×2 Inch Lead-centered Diaphragm)	Total Radiation (6×6 Inch Diaphragm)
Intensity in air	14.3 r/min.	5.6 r/min.	19.9 r/min.
Relative intensities	100%	39%	139%
Relative intensities for same quality of radiation*	100%	35%	132%
Effective wave length (from 0.25 mm. Cu)	0.155 Å.	0.170 Å.	0.160 Å.
Half value layer	1.01 mm. Cu	0.90 mm. Cu	0.96 mm. Cu
Filtration equivalent from standard copper absorption curve	0.55 mm. Cu	0.43 mm. Cu	0.50 mm. Cu

* Values calculated from Figure 3 for actual filtration of 0.5 mm. Cu for direct radiation, 0.62 mm. Cu for scattered radiation, and 0.55 mm. Cu for total radiation.

curve (Fig. 3). The initial filter for the standard curve is 4.78 mm. Pyrex glass. The actual initial filter for the total radi-

Phantom Measurements.—Comparative measurements in a rice phantom for the direct and total radiation could be made for

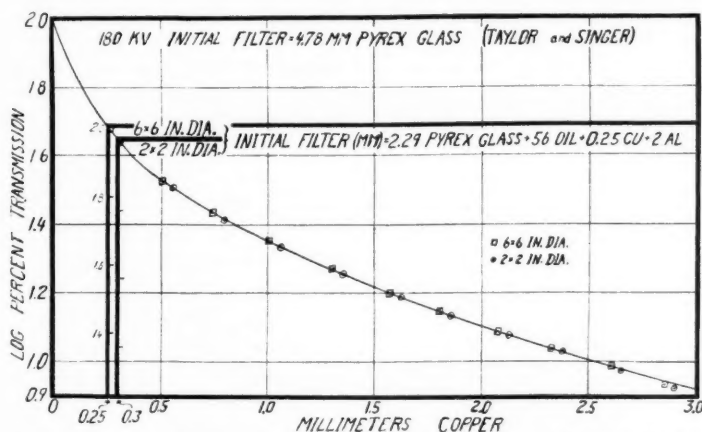


Fig. 3. Copper absorption curve. The curve is from data published by Taylor and Singer. The points are the experimental data obtained with the 6 × 6 inch and 2 × 2 inch diaphragms.

tion and the direct radiation was 2.29 mm. Pyrex glass + a minimum of 56 mm. oil + 0.25 mm. Cu + 2 mm. Al. The initial filtration as determined from Figure 3 is equivalent to, in addition to the 4.78 mm. Pyrex glass, 0.3 mm. Cu for the direct radiation, and 0.25 mm. Cu for the total radiation. This shows that, with the same actual filtration, the total radiation is softer than the direct.

Measurements to determine the entire absorption curve for the scattered radiation (lead-centered diaphragm) were not made because of its small intensity. However, since the measurements made with a few filters showed that the intensity of the scattered radiation for any given filter was equal to the difference between the intensities of the total and direct radiations for that filtration, the values for the copper absorption curve for the scattered radiation can be calculated from the data for the other two curves. The curve obtained by this method coincided fairly well with the 180 kv. (constant) standard curve and gave an initial filtration equivalent to 0.18 mm. Cu. This initial filtration equivalent shows that the scattered radiation is softer than either the total or the direct.

only a 5 × 5 cm. field because the dimensions of the beam of direct radiation were not great enough to cover a larger field. The ratio of the intensity on the surface of the phantom to the intensity in air for 0.5 mm. Cu filtration was practically the same for the two beams, being 115 per cent for the direct beam and 116 per cent for the total beam. The absolute surface intensities, however, were 40 per cent greater for the total beam than for the direct. As shown in Figure 4, there is some difference in the isodose curves for the two beams; the curves for the total beam differ from those for the direct beam in that they tend to be a little flatter near the surface and extend farther outside the edge of the beam of radiation. This difference would be expected because the additional radiation present in the total beam, since it has been scattered by the oil surrounding the tube, strikes the surface of the phantom at a smaller angle than the radiation in the direct beam. The relative depth intensities are greater for the direct beam than for the total beam; this difference is chiefly due to the fact that the additional radiation present in the total beam, because of the angle at which it is travelling, will have

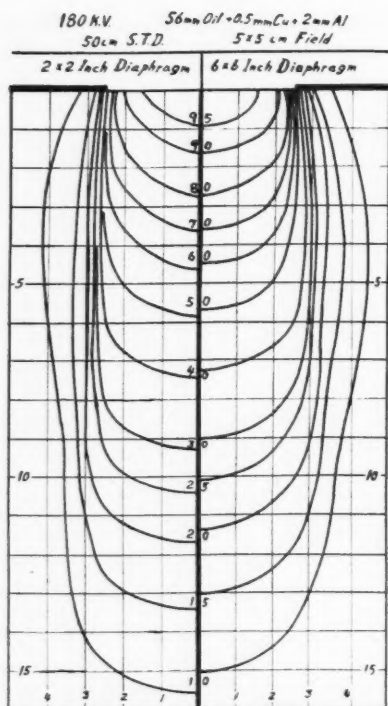


Fig. 4. Half of two sets of isodose curves for a 5×5 cm. field. One set was obtained with a 2×2 inch and the other set with a 6×6 inch diaphragm.

more relative effect near the surface than at a depth. The harder quality of the radiation in the direct beam would also cause it to have higher relative depth intensities, but the slight difference in quality would not cause as much difference as is shown in Figure 4.

DISCUSSION

This study has shown that, for a tube immersed in a large tank of oil, the rate at which radiation was delivered to a small field was much greater when a diaphragm with a large opening was used than when a small opening was used. For a filtration of 0.5 mm. Cu, the intensity measured in air was 39 per cent greater when using the 6×6 inch diaphragm than when using the 2×2 inch diaphragm. This must be taken into consideration when calculating doses used in therapy if they are calculated from intensity measurements made in air. If more

than one diaphragm is used the intensity of the radiation must be determined for each. If one large diaphragm is always used, and the size and shape of the area to be irradiated is defined by means of lead sheets and leaded rubber, there will be one less variable factor than if diaphragms of different sizes are used. The use of cones will not affect the intensity if the end of the cone which attaches to the tube tank is the same shape and size as the diaphragm ordinarily used, but the use of "cylindrical cones" of small cross-sectional area will reduce the intensity.

From Figure 3 it is seen that, if the filtration were to be increased by 0.05 mm. Cu for the radiation passing through the large diaphragm, its quality would be the same as that of the radiation passing through the small diaphragm. Calculations of the intensities of the two beams with their filtrations adjusted so that their qualities would be the same show that the intensity with the 6×6 inch diaphragm is 32 per cent greater than with the 2×2 inch diaphragm.

The radiation coming through the 2×2 inch diaphragm has been called direct radiation. Actually this beam contains some scattered radiation. The dotted lines in Figure 1 indicate the volume in which radiation can originate, or be scattered, and reach the ionization chamber. Radiation scattered by oil outside of this volume, but near to it, might reach either end of the ionization chamber. Radiation might possibly be scattered several times by the oil before reaching the ionization chamber, and the point at which it was first scattered might be quite far from the indicated volume. Also, there would probably be a considerable amount of radiation scattered through a small angle; a great deal of this would reach the ionization chamber regardless of whether or not it had been scattered, but if it had been scattered it would have lost part of its energy and would be softer in quality.

One fact which indicates that a considerable proportion of the radiation which passes through the 2×2 inch diaphragm

has been scattered, and thereby made softer, is the low value for the initial filtration equivalent obtained from Figure 3. An inch of oil used as a filter is generally considered to be equivalent to approximately 0.25 mm. Cu; hence it would seem that the initial filtration equivalent should be approximately 0.75 mm. Cu instead of 0.3 mm. Cu. This decrease in initial filtration equivalent indicates that a considerable part of the radiation has been scattered.

It would be desirable to determine the intensity and quality of the radiation without any oil in the tank and to compare such results with those already made. But due to the constant use of the machine for therapy and the short distances between the ends of the tube and the walls of the tank (insufficient electrical insulation without oil) it was not possible to make such measurements. Nor is it possible to make any accurate comparisons with data reported in the literature because of the difference in operating conditions. From comparisons it has been possible to make, it would appear that for radiation of the same quality the intensity of the radiation is greater for the tube surrounded by oil, when a large diaphragm is used, than it would be if the tube were surrounded by air.

If, by surrounding a tube with a rather large volume of oil, a greater intensity of radiation of the same quality can be obtained, the efficiency of an x-ray machine would be increased. To accomplish this the tube housing should have a very thin layer of oil below the tube in the area through which the useful direct radiation would pass and a large volume of oil around the cone of direct radiation. This large volume of oil around the cone of direct radiation would have no effect on the direct beam of radiation, but it would scatter radiation into the useful beam which otherwise would be wasted. By building in more filtration for the scattered radiation than for the direct, both components of the final beam could be made to have

approximately the same quality. The difference in shape of the isodose curves and the decrease in the relative depth intensities, as shown in Figure 4, which might result from surrounding the tube with oil, are objections which might counteract the benefits of the increased efficiency.

SUMMARY

Of the useful beam of radiation from an x-ray therapy tube immersed in a large tank of oil, from 25 to 32 per cent of the intensity of the beam passing through a large diaphragm has been found to be due to radiation which does not come directly from the target of the tube. Most of this extra radiation has been scattered into the useful beam by the oil surrounding the tube. This scattered radiation is of a softer quality than the direct radiation but can be changed to radiation of the same quality by increasing its filtration by 0.12 mm. Cu.

If doses in radiation therapy are calculated from intensity measurements made in air, intensity measurements should be made for each size of diaphragm which is to be used if the tube is surrounded by oil.

Because the radiation scattered by the oil has more effect near the surface of a phantom than at a depth, the relative depth intensities are reduced by the presence of this scattered radiation.

A tube housing in which the tube is immersed in oil might be constructed so that there would be a large volume of oil surrounding the useful beam of radiation which would scatter a considerable amount of radiation, that would otherwise be wasted, back into the useful beam.

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NEW DEVICES

TECHNICAL DATA CONCERNING THE GEIGER COUNTER

By ROBERT B. TAFT, M.D., B.S., M.A., F.A.C.R.,
Charleston, South Carolina

As no description of a "Geiger Counter" can be found in medical literature, an investigator wishing to build this instrument has to waste much time in testing various circuits. For that reason this paper seems warranted. The photograph and complete wiring diagram show a successful, self-contained instrument. The author has made certain modifications in the usual circuits, has arranged for complete AC

The voltage supplied to this tube is not critical but must be in excess of 750 volts direct current. With the proper circuit, this can be gotten very easily from a small transformer such as is used in any radio broadcast receiver. The voltage from this transformer is usually regarded as about 320 but, as there are two secondaries, each giving that voltage, they can be connected in a series and the voltage rectified half wave with an 82 tube the plates of which are connected in parallel. When a condenser of 2 mf. (working voltage 2,000 v.) is placed across this, the voltage is raised to about 850 and, as the drain is so small, there is

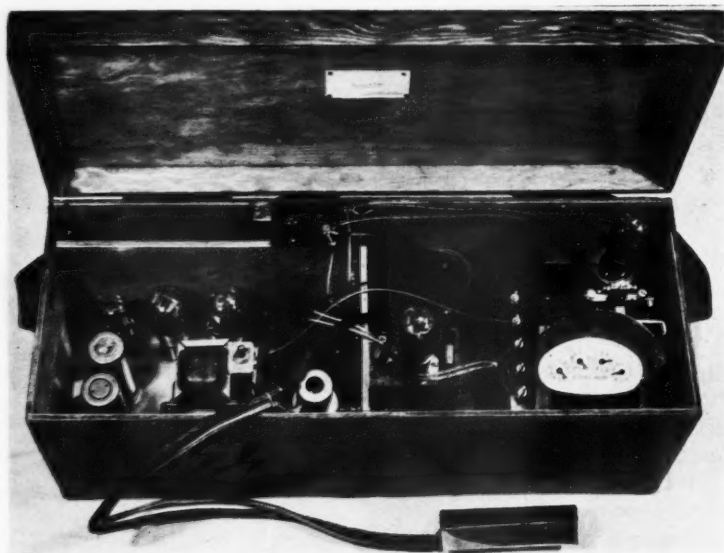


Fig. 1.

operation with elimination of all batteries, and, with the exception of the tube and recording counter, has used only standard radio receiving parts which are inexpensive and easily obtained in any city. Otherwise, no originality is claimed.

The success of this instrument depends on the "Stratosphere Tube" developed by Dr. Gordon L. Locher, of Philadelphia, for cosmic ray determinations, consisting of a small glass tube filled with gases and partially exhausted. When arranged with proper voltage supply, amplifying system, and recorder, it is an extremely sensitive device for the determination of radiation.

practically no fluctuation. The 82 tube is somewhat overloaded but it seems to stand up continuously without damage.

The output from the Locher Tube is fed through a 0.0001 mf. condenser into the amplifying system, but it is necessary that the tube, condenser, and the first amplifying tube be completely shielded in grounded metal covers.

The amplifying circuit consists of a small public address system with one pre-amplifier ahead of it. The loud speaker is well adapted for demonstration use and for conditions in which the radiation impulses are too rapid to be recorded.



Fig. 1. Postero-anterior view

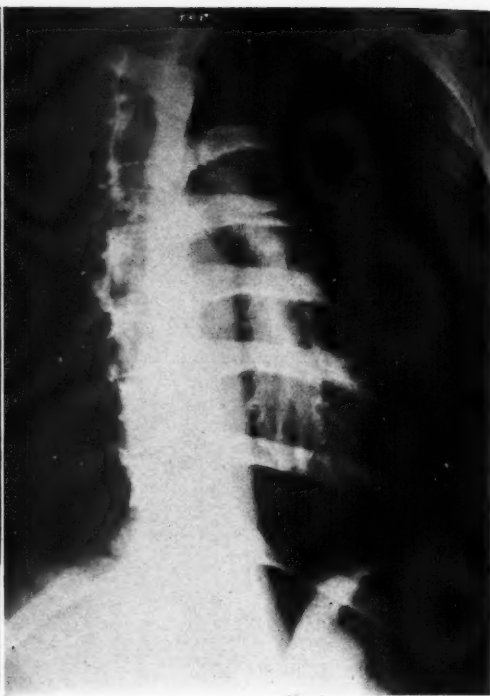


Fig. 2. Postero-anterior view.

tion, with the head turned to the left, the left arm flexed around the head, and the right arm alongside the body. The patient is rotated about ten degrees to the right, which is all that is necessary to project the sternum just to the left of the vertebral column. This gives an approximate postero-anterior view. One will find that rotation of twenty-five degrees or even of twenty-two and a half degrees, as suggested by Rhinehart, will throw the sternum into an oblique view.

The x-ray tube should be centered over the middle of the sternum and the rays should be directed perpendicular to the cassette. Intensifying screens and the Potter-Bucky diaphragm are used, and it is preferable to have the films taken stereoscopically at a distance of thirty-six inches, using a cone large enough to cover a 10×12 film. We have found that 300 milliamperes-second exposures are satisfactory, with penetration sufficient to bring out detail (Figs. 1 and 2).

EDITORIAL

LEON J. MENVILLE, M.D., *Editor*

HOWARD P. DOUB, M.D., *Associate Editor*

COMMENTS ON CANCER EXPLOITATION AND CANCER CONTROL IN THE U. S. A.

Cancer—the mysterious, cancer—the unknown, cancer—the fertile field of the charlatan, the advertising quack and the unscrupulous physician—has been for many years, and still remains, a challenge to scientific medicine. Frankly, we have as yet very little to offer, and we have steadfastly acknowledged our limitations in the cure of this universal affliction. We have attempted in an honest and altruistic way to tell the truth about cancer, to encourage our professional brothers in maintaining a spirit of hopeful confidence for the ultimate control of this disease, and to plead with the cancer-afflicted public to seek proper medical advice at a sufficiently early period to insure the arrest and possible cure of the disease.

In the meantime, what is taking place to minimize our efforts? In Missouri, in North Carolina, and in other States, institutions governed by profit-seeking and wholly mercenary individuals are advertising, throughout the land, cures for cancer by methods which belong to the Dark Ages. There are in use fearsome caustic pastes and other devilish contraptions, with which to destroy warts, moles, and other surface growths of more or less serious nature, and even advanced cancer of the breast. These efforts produce, of course, a painful destruction of a great many perfectly innocent lesions, but usually fail in a cure of the really malignant disease.

In Mexico, an ousted cancer quack from the United States, with the accompaniment of song and music, tells through a powerful radio broadcasting station of his "cures" by methods similar to those just mentioned. In Los Angeles, a naturopath, or drugless healer, supported by a leading newspaper, "cures" cancer with orange juice at five dollars or more per dose. Even respectable (?) doctors of medicine and surgery are injecting serums and high priced metallic colloids into the anatomy of the cancer-afflicted, who are led to believe that cures can be obtained in that manner. And so on and forever goes this ungodly exploitation of the cancer sufferers.

The medical profession is therefore not entirely blameless, for there are altogether too many who, knowing better, will keep helpless patients in a hopeful frame of mind by giving pills, potions, and injections of all sorts, including enzymes, serums, and colloids of various kinds at so much per, knowing full well the total inadequacy of such agents to effect a cure or even attain a reasonable degree of palliation.

What is the regular medical profession doing to combat this colossal humbug? Practically nothing! True, there are a few more or less sustained efforts by such groups as the American Medical Association, the American College of Surgeons, the American Society for the Control of Cancer, and several state societies with Cancer Commissions that are doing good work to educate the members of their own profession, but not one single concerted effort is made by the medical profession as a whole to corral the quacks. Is it because our profession is living in the past, when common honesty bound people more closely together and the physician had the respect and confidence of his community? Is it because we are still living in that time of sacred memories that we are blind to the ways of the present commercialized civilization? Is it not a cold fact that we have been content to go on in a state of imbecilic apathy secure in our own simple-minded faith until we are now surrounded by hordes of irregular practitioners, faddists, and cultists who, in the eyes of the law, are our equals, and, in a great many ways in the eyes of the general public, our superiors?

It is well enough for us to feel, and to be, above all questionable methods of procedure in the conduct of our professional obligations, but unless the regular medical profession awakens to a realization of what is going on in this politically commercialized world, it will itself be forced to embrace this type of racketeering which has become an uncontrollable international disease. Not only against cancer quacking must we guard our portals, but also

against that insidious octopus which threatens to extend its tentacles in an all-absorbing attempt to regimentate the entire medical profession into a subversive union. While this is a degeneration from our subject, it has a vital bearing upon all of us and we must heed the call to arms. Let us, therefore, briefly cogitate upon the probable trend of events if the foregoing remarks attain a reasonable degree of truth.

The regular medical profession, with its waning powers to influence medical legislation or to sway public opinion, is faced with the humiliation of taking orders from some political leech as to how it shall conduct its private practice or how it may continue on in its time-honored and sacred professional tenor, and how much it shall charge the private and public patient for any and all medical service. This is not an imaginative outburst. You men of medicine, just look around and see what is going on in your own town, county, State, and beyond, and you will find that legislative bodies everywhere are importuned by laymen to pass vicious bills enacted solely for the purpose of undermining the very foundation of medicine. If this move is successful, we will be compelled to accept for our medical services that pittance grudgingly allowed us by the particular ward heeler, demagogue, or communistic nincompoop in supreme control of every individual medical community.

Attention is drawn to a recent article wherein suggestions are made by the undersigned to establish a national board of cancer control. If this or some similar plan were to be worked out, it would not be long before an awakened medical profession would have the situation well in hand.

In conclusion, it would seem highly essential, in view of the foregoing, that definite steps be taken by the cancer-minded members of our profession at once, in order to co-operate and align themselves with every legitimate cancer study and control organization, such as already alluded to, so that there may eventuate a strong authoritative central organization, powerful enough to make its voice heard and its messages obeyed over our whole country. Then and only then may we expect a sustained cancer control program which will yield, I firmly believe, in one decade, a 50 per cent reduction of the present known cancer incidence.

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ALBERT SOILAND, M.D.

COMMUNICATIONS

AMERICAN RADIUM SOCIETY

Twentieth Annual Meeting, May 11, 12, 1936

The American Radium Society has just closed an Annual Meeting which has been outstandingly successful, and which was attended by most of the leading radium therapists and physicists of the country. The program follows:

"The Measurement of Tissue Doses in Terms of the Same Unit in X-ray and Radium Therapy," G. Failla, D.Sc., New York City.

"The Experimental Determination of Tissue Doses in Teleradium Therapy," Edith H. Quimby, M.A., and L. D. Marinelli, M.A., New York City.

"The Present State of Physical Radium Dosimetry," Otto Glasser, Ph.D., Cleveland.

"Protracted Irradiation by Radium," Hayes E. Martin, M.D., and William S. MacComb, M.D., New York City.

"Limitations of Radium Therapy in Cancer of the Cervix," Palmer Findley, M.D., Omaha.

"Clinical Results and Histologic Changes Noted in the Radiation Treatment of Corpus Cancer," A. N. Arneson, M.D., St. Louis.

"The Calculation of the Dosage in the Treatment of Carcinoma of the Cervix," Charles DeF. Lucas, M.D., Charlotte, N. C.

"Serious Complications Encountered during Radium Treatment of Carcinoma of the Uterine Cervix," H. H. Bowing, M.D., and R. E. Fricke, M.D., of Rochester, Minn.

"A Method of Treatment of Cancer of the Cervix" (motion picture), Hyman Strauss, M.D., Brooklyn, N. Y.

"Early Experiences with Radium" (Jancway Lecture), C. F. Burnam, M.D., Baltimore; introduction by Douglas Quick, M.D., New York City.

"The Radiation Treatment of Carcinoma of the Breast Recurrent after Operation," Sanford Withers, M.D., Denver.

"A Study of Tissue Dosage and Radiation Effect in Cancer of the Breast Treated by X-rays and by Teleradium Therapy," F. E. Adair, M.D., E. L. Frazell, M.D., and Edith H. Quimby, M.A., New York City.

"Microscopic Grading: Its Interpretation, Limitations, and its Relation to Radiosensitivity," W. C. MacCarty, M.D., Rochester, Minn.

"The Relative Importance of Histological

Analysis in Tumor Therapy," F. C. Helwig, M.D., Kansas City.

"Tissue Changes Resultant from Radiation," L. H. Jorstad, M.D., St. Louis.

"Advanced Cancer about the Head," C. L. Martin, M.D., Dallas, Texas.

"The Educational Advantages of the Tumor Clinic," G. M. Dorrance, M.D., Philadelphia.

"Evaluation of Radiation in the Treatment of Uterine Fibroids and Menorrhagia," C. F. Burnam, M.D., Baltimore.

"Radium *versus* Roentgen Ray in the Treatment of Benign Uterine Bleeding," John W. Cathcart, M.D., El Paso, Texas.

"The Use of 200- to 600-millicurie Radon Pack in the Treatment of Malignancy," W. E. Howes, M.D., Brooklyn, N. Y.

"The Use of Radium Element Seeds in the Treatment of Cancer," G. T. Pack, M.D., New York City, and L. R. Taber, M.D., Paterson, N. J.

"Protective Factors in the Preparation and Handling of Gold Implants and Other Radon Applicators," Wilhelm Stenstrom, Ph.D., and C. E. Nurnberger, Ph.D., Minneapolis.

"Therapeutic Use of Various Solutions of Radium Emanation: Preliminary Report," I. I. Kaplan, M.D., New York City.

From a perusal of the above list of papers it is plain to see that every one doing radium therapy either was or might with advantage have been present at the meeting.

INTERNATIONAL CANCER CONGRESS

The Radiological Society of North America has joined the Union Internationale contre le Cancer and has paid the annual dues. Each member of the Society has the right to attend the Congress in Brussels, Sept. 20 to 26, 1936.

However, the individual who wishes to present a paper at the Congress must pay an "inscription fee" of 100 Belgas or about \$17.00, which he can get at his own bank by buying Belgian exchange.

If any member wishes to join the Congress, he should send 100 Belgas to Mr. H. Schraenen, National Executive Committee General Secretariat, 13 rue de la Presse, Brussels, Belgium.

ILLINOIS RADIOLOGICAL SOCIETY

The Illinois Radiological Society met at 10:30 A.M. on Sunday, April 26, 1936, at Champaign, Ill. After hearing the conclusions of the Committee in charge of the study of the constitution of the Illinois Society of Radiographic Technicians, it was moved and approved that the Illinois Radiological Society endorse the constitution of the Illinois Society of Radiographic Technicians.

A film clinic followed and interesting cases were presented by Dr. Morgan, Dr. Kariher, Dr. Gianturco, and Dr. Jewell. Dr. James H. Finch presented an apparatus for the reduction of fractures.

After dinner, Dr. C. H. Warfield gave a most complete discussion of the radiological aspects of bone tumors. Dr. C. Gianturco presented two instruments for the radiographic visualization of the optic canals and the temporal bone in Stenvers position.

MINNESOTA RADIOLOGICAL SOCIETY

The annual meeting of the Minnesota Radiological Society was held in connection with the meeting of the Minnesota State Medical Association at Rochester, Minn., May 4, 1936.

The Russell D. Carman Memorial Lecture was delivered by Dr. Willis F. Manges, of Philadelphia, on the subject, "Foreign Bodies and the Use of X-ray Examination in Their Localization and Removal."

At the annual dinner Dr. Manges addressed the members of the Society on "The Future of Radiology."

Election of officers for the coming year resulted as follows: *President*, Dr. J. Richards Aurelius, of St. Paul; *Vice-president*, Dr. Walter H. Ude, of Minneapolis; *Secretary-Treasurer*, Dr. Leo G. Rigler, of Minneapolis.

NOTICE OF CORRECTION

It now comes to the attention of Dr. Ernst Lachmann that there has been an error in quoting Dr. H. R. Schinz in the paper entitled "The Roentgen Diagnosis of Osteoporosis and its Limitations," in *RADIOLOGY*, February, 1936. On page 168, line 21, from the top of the first column appearing under heading

(3), should read "1.9 times that of its surroundings," instead of "nine times that of its surroundings."

DR. RUDOLPH GRASHEY

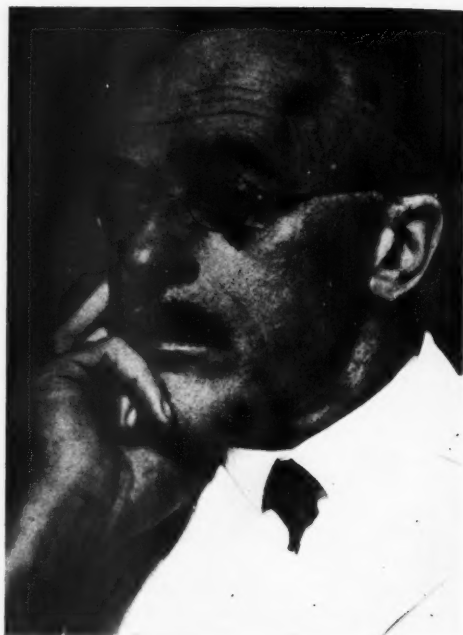
Dr. Rudolph Grashey, Professor of Roentgenology at the University of Cologne and Director of the Municipal Roentgen and Light Institute at the Citizens' Hospital, celebrated his sixtieth birthday on Feb. 24, 1936. Rudolph Grashey is a pioneer in roentgenology on the Continent and well known to the radiologists of this country, particularly as Editor of "Fortschritte auf dem Gebiete der Röntgenstrahlen." It was founded by Albers-Schönberg, who died as a martyr of his chosen specialty and fifteen years ago Grashey became his successor. The latter also founded "Röntgenpraxis," which is now appearing in its eighth volume.

In honor of Grashey's sixtieth birthday, "Fortschritte" published a Festschrift, edited by W. Baensch (Leipzig), F. Haenisch (Hamburg), and H. R. Schinz (Zürich), as the March issue of Volume 53. It contains 57 papers covering diagnostic roentgenology, radiobiology, radiation therapy, physics, and technic. Radiologists of many nations are found among the contributors; this country is represented by A. C. Christie (Washington) and G. Failla (New York). "Strahlentherapie," in the issue of Feb. 26, 1936, also acknowledges the outstanding accomplishments of Grashey in the science of radiology. We join our colleagues on the Continent in wishing that he may continue his invaluable services to humanity for many years to come.

ERNST A. POHLE, M.D., Ph.D.

BOOK REVIEW

A TEXTBOOK OF ROENTGENOLOGY: THE ROENTGEN RAY IN DIAGNOSIS AND TREATMENT. By BEDE J. MICHAEL HARRISON, M.B., CH.M., D.M.R.E. (Cantab.), F.A.C.R., Director of Department of Roentgenology, Vancouver General Hospital, Roentgenologist to Vancouver Public Health Institute for Diseases of the Chest. A volume of 788 pages, 238 illustrations. Published by



DR. RUDOLPH GRASHEY

William Wood & Company, Baltimore, Maryland, 1936. Price, \$10.00.

This comprehensive work presents roentgenology in a novel and interesting manner. The author approaches roentgen diagnosis and treatment through pathology, with adequate remarks on normal anatomy interposed. This method makes the book of particular value to students of roentgenology, both undergraduate and graduate. To the average roentgenologist the method is questionable, as it entails an extensive repetition of obvious data on anatomy and pathology with most of which he is thoroughly familiar. Furthermore, the detailed treatment of these related subjects, a repetition of material which is readily available in other special texts, has reduced the amount of space available to the primary subject of the book, namely, roentgenology.

There are some 788 pages, by far the largest book in English published in recent years on this subject. The volume is remarkably complete, all fields of roentgen diagnosis and therapy being touched upon—in some cases perhaps too lightly. Even the rarest of diseases are briefly described and data are presented on

even the most recent contributions to roentgen diagnosis. On the other hand, the detailed descriptions of the roentgen findings in any one disease are very limited.

The author is to be commended for his instructive chapters on general principles of radiology, physics, radio-physiology and biology, technic, and the nature of roentgen evidence. The text on the whole is very readable and concise, and in these chapters the approach to roentgenology is made clear in an interesting, original manner.

Certain specific criticisms must be made. The statements anent the value of roentgen therapy in numerous conditions such as hyperacidity and gastric ulcer are loose and uncritical. The conclusions expressed as to the results of radiation therapy in other diseases, such as hyperthyroidism, are unduly optimistic. An unfortunate impression is conveyed that roentgen therapy is effective in many diseases in which the beneficial results have never been effectively proved.

There is a certain disproportion in space allotments which leads to undue brevity in treating important subjects. One short paragraph on bronchial neoplasms hardly seems adequate. There is less than a page devoted to bronchiectasis. Pulmonary tuberculosis is

dealt with much more fully, but here again the discussion is largely devoted to clinical findings and the classification of the disease rather than to the roentgen diagnostic signs. On the other hand, undue emphasis is placed on such a recent procedure as hepato-lienography, even though its value and limitations have not yet been clearly defined.

The illustrations are much too few for so complete a book and are not very well reproduced. There is no reference to the illustrations in the text so that they appear to be of a separate nature. In many instances the illustrations are far removed from that portion of the text in which the condition they represent is discussed. The book contains no bibliography or any attempt at references to the literature, although it is obvious that the author is thoroughly versed in the most recent contributions on roentgen diagnosis and therapy.

Consideration of the book as a whole suggests that it may have a valuable place in medical literature. It renders to the physician a bird's-eye view of the value of roentgen diagnosis and treatment in the various diseases which he may encounter in his practice. It gives the student of roentgenology and the roentgenologist a correlation in one volume of anatomy, pathology, and roentgenology.

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